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Observations on the pathology of hydrocephalus

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PREFACE

THE Medical Research Council are glad to include in their *Special Report Series* this important study by Professor Dorothy Russell, who was a member of their scientific staff until 1946, when she was appointed Director of the Bernhard Baron Institute of Pathology at the London Hospital and Professor of Pathology in the University of London.

A monograph on hydrocephalus from an authoritative source has long been needed. For 30 years we have been in possession of the basic knowledge on which a workmanlike structure could be built, but time was required to accumulate a sufficient variety of examples with which to illustrate not the essential condition but its many and various causes. To travel from the observations of Vesalius, Morgagni and Robert Whytt to those of the present day is indeed a prodigious scientific journey, and it is not the least interesting fact that the greater part of the progress recorded has been made with great acceleration in our own times.

The particular value of Professor Russell's study, which is an expansion of a series of three lectures given at the Nuffield Institute for Medical Research, Oxford, in 1942, lies in the thoroughness of her survey of the morbid anatomy. She finds no grounds for retaining the overworked and misused word "idiopathic" in connection with the origin of hydrocephalus ; on the contrary it is her view that in every case some form of obstruction can be demonstrated in the cerebrospinal pathway.

Congenital hydrocephalus is usually due to a malformation, the most frequently observed of these being (1) the so-called "atresia" of the aqueduct: really a forking of the channel, a condition quite distinct from "gliosis", with which it has often been confused; and (2) the Arnold-Chiari malformation associated with spina bifida. The variations in the Arnold-Chiari malformation with different grades of spina bifida are examined at some length, and the theory of traction, favoured by almost every recent writer as the cause of the malformation, is found untenable. It is hoped that the discussion of this subject may prove helpful in guiding surgeons in their selection of the operable examples of spina bifida. Professor Russell thinks that "gliosis" of the aqueduct is probably the result of a low-grade inflammatory process, and not a maldevelopment. She finds some evidence that a widespread disturbance of the relations of the ependyma and subependymal glia occurs in these cases, and that obstructive effects are manifest in the aqueduct solely on account of its small size.

The development of hydrocephalus often begins in infancy, and the view is gaining acceptance that meningitis, perhaps undiagnosed at the time and due to organisms that seldom become established in the meninges of the adult, is probably its most frequent cause at this age. Of all forms of hydrocephalus this is the most obscure, and it is the more difficult to elucidate because a latent period of variable duration usually elapses before the hydrocephalus becomes apparent. But it is not only for these reasons that a considerable part of the monograph has been devoted to meningitis and its sequels. Modern chemotherapy has reduced the fatality rate even of those forms of meningitis which

previously were nearly always lethal, and the improved treatment it offers for infantile meningitis raises the hope that we may increasingly be able to prevent the subsequent development of hydrocephalus. To do this, however, early recognition and optimum treatment of the meningitis will be necessary; otherwise, by saving lives that would formerly have been lost, we may multiply rather than reduce the frequency of residual lesions. The effect on the incidence of such lesions of the power of streptomycin to prolong life in a proportion of cases of tuberculous meningitis has yet to be seen.

It may be added that syphilis, so often given pride of place in the text-books as a cause of infantile hydrocephalus, does not figure in Professor Russell's material except, very rarely, as a cause of hydrocephalus in the adult.

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Note to 1966 Reprint

THIS reprint does not contain any revision of the text of the report. However, a later contribution to the subject by Professor Russell has been included in the volume as an appendix, which serves the purpose of correcting and amplifying certain views on the causation of hydrocephalus that are expressed in the monograph. This paper forms chapter IX of volume XXXIV of the Research Publications of the Association for Research in Nervous and Mental Diseases (published in 1954 by Williams and Wilkins Co., Baltimore), and the Council are most grateful to the Association for permission to reproduce it here.

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OBSERVATIONS ON THE PATHOLOGY OF HYDROCEPHALUS

by

DOROTHY S. RUSSELL, Sc.D., M.D., F.R.C.P.

CHAPTER I

INTRODUCTION

THIS study of the pathology of internal hydrocephalus is based upon observations made during the past seventeen years at the Bernhard Baron Institute of Pathology, the London Hospital, and, during the war years, at the Nuffield Department of Surgery, Oxford. During these years I have had the great advantage of working with Sir Hugh Cairns, Dr. Joe Pennybacker and Mr. D. W. C. Northfield and their assistants. A large proportion of the cases passed through the hands of these neurosurgeons. But many interesting examples of hydrocephalus were derived from other sources and I am indebted for supplementary material to a number of my medical colleagues, especially in the obstetric and pædiatric departments. The recognition, at postmortem examination, of the early and latent grades of disease that escape clinical recognition forms a necessary background to the study of the more advanced cases. My indebtedness therefore lies not only towards the neurosurgeons already mentioned, and to Mr. Charles Donald who worked with me during the earlier years, but also to the other clinicians of the London Hospital and the Radcliffe Infirmary, Oxford, and to others, mentioned in the text, who have generously added to my store. I wish to take this opportunity of thanking them.

Collectively the cases have provided me with material which I feel to be exceptional in its variety and extent. This, and the rather vague treatment of the pathology of hydrocephalus in the current textbooks and other standard works, have prompted the preparation of the present study. In this I have made no attempt to deal with the question of treatment, and the clinical manifestations of disease are but briefly recapitulated in order to give some background to the pathological study. A survey of the collected cases showed, as might be expected from the circumstances, a great predominance of intracranial tumours. This, and the repetition that would be entailed by giving an account of each individual example in the complete series, has made it expedient to redress the balance by selecting the cases to be described in the text. It was therefore decided to illustrate each different type of pathological condition by picked cases from the series, with the general aim of providing as complete a survey of the morbid anatomy as possible. Where necessary a few gaps have been filled in from the literature. The reports and stored microscopical slides of the Bernhard Baron Institute have provided certain additional cases; some of these, described by Professor H. M. Turnbull, have proved of great value and I wish to express my appreciation of his careful records.

The cases annotated in the text are derived from the records of the London Hospital unless otherwise indicated; those from the Radcliffe Infirmary, Oxford, carry the initials R.I. before their serial registration numbers.

Historical Notes

The clinical observation of hydrocephalus, with its striking cranial deformity, is doubtless as old as medicine itself. But, in the brief historical notes that follow, no attempt will be made to trace records into ancient times since, on the authority of Morgagni (1761), it appears that the physicians of earlier periods had somewhat vague ideas as to where in the brain and its integuments the fluid accumulated. It was most generally supposed that the fluid lay external to the brain. Vesalius (1514-64), iconoclastic in this as in other matters, appears to have given the first clear account of internal hydrocephalus. The relevant passage, from Chapter V of Book I of the "Opera Omnia" (1725), for the translation of which I am indebted to Mrs. Isobel Henderson of Somerville College, Oxford, is as follows:

"Galen declared that this shape (of skull) can, indeed, be conceived as existing in another world, but cannot exist in nature. Nevertheless, a boy may be seen to-day in Venice, deformed in many of his parts and quite insane, with a head of this shape. And, in fact, a beggar who goes about at Bologna has a head which is square, but a little broader than it is long Besides, at Genoa there was a small boy who was carried round from door to door by a beggar-woman, and was soon afterwards exhibited by play-actors in the most noble province of Brabant in Belgium: and his head bulged out on both sides and was bigger than two men's heads. Now I think that that boy suffered from a disease like that which I observed at Augsburg in a two-year old girl whose head had grown in seven months, more or less, to such a size that I never saw any man's head which was not surpassed by it in bulk. This disease was what the ancients called hydrocephalus, from the water which is stored in the head and gradually collects. In this girl's case, however, the water had not collected between the skull and its outer surrounding membrane,* or the skin (where the doctors' books teach that water is deposited in other cases), but in the cavity of the brain itself, and actually in the right and left ventricles of the brain. The cavity and breadth of these had so increased—and the brain itself was so distended—that they contained about nine pounds of water, or three Augsburg wine-measures (so help me God). Moreover, just as the brain in the crown of the head was of an almost membrane-like thinness, and formed in a manner of speaking one continuous body with its own thin membrane, so also the skull was quite membranous—but, at the same time, its bony seat was still of the size of the girl's skull before her head began to grow abnormally. The manner of this was much the same as that which we perceive in new-born children, in the structure of the frontal bone and the bones of the head, which are normally contiguous with each other, but in quite small children are observed to have a considerable gap, with a stretch of membrane. The cerebellum, nevertheless, and the entire base of the brain, were in their natural state ; and so were the extensions of the nerves. And I found no water in any other places but in the ventricles of the brain, which were enlarged to the extent that I have stated ; and the girl had the full use of all her senses up to her death. I inspected her a few days before her death, and then, whenever her head was moved by the persons attending, and was somewhat raised, however slightly, at once a severe cough troubled the girl, with difficult respiration, an extraordinary redness of the whole face, a suffusion of blood, and a flow of tears. The condition of the rest of her body was moderate: her joints, though loose and weak, were not slack ; there was no marked emaciation, nor any watery swelling in the limbs, nor signs of epilepsy or any kind of convulsion. The liver, which was examined soon after death, appeared rather pale, and a good deal harder and more shrunken than a natural liver would otherwise be ; the spleen, however, was extremely large and conspicuously soft, just as if it had for some time past been performing the functions of the liver. Indeed I, with the doctors who were present, found nothing more surprising than the fact that such a great force of water had been accumulated for so long in the ventricles of the brain without more extensive symptoms."

Morgagni (1761) confirmed the accumulation of fluid within the ventricles in hydrocephalus. He pointed out that the brain tissue may be reduced "almost to the thinness of a membrane" and that the surgeon engaged in paracentesis may think he perforates the dura only but in reality perforates the brain. Morgagni also recognized that, while hydrocephalus in the foetus and young

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* The text reads: *Quamquam ea non inter calvariam et exterius ipsam succingentem membranam, aut cutem (ubi alias aquam reponi medicorum libri docent) huic puellae fuerit collecta.* It is clear that *exterius ipsam* (*sc. calvariam*) *succingentem membranam* is meant to refer to the pericranium.

infant was attended by enlargement of the head, it also occurred in adults when the head was not enlarged. Though this is now general knowledge, in the eighteenth century, according to Morgagni, most observers would not credit the existence of hydrocephalus without enlargement of the head.

Meanwhile a contemporary of Morgagni's in this island, Robert Whytt (1768), had studied a series of cases in young subjects ranging for the most part between the ages of 2 and 15 years, with autopsy in ten instances. He made a clear distinction between internal and external hydrocephalus. In all his dissections he found an increase of fluid in the lateral ventricles, and sometimes in the third and fourth. He specifically states that he "never met with water between the dura mater and the brain, between the hemispheres of the brain, or immediately above the corpus callosum". In none of his patients was the size of the head increased. He correlated this excessive accumulation of fluid in the ventricles with fever, squint, and photophobia, together with paralysis of the facial muscles. There can be little doubt that meningitis, and in particular tuberculous meningitis, was the predominant ætiological factor in his cases. Charles West (1848) distinguished between acute and chronic hydrocephalus. The acute form was due to cerebral inflammation in scrofulous subjects, and it is clear from his descriptions of the brain that the condition was tuberculous meningitis. He found that chronic hydrocephalus was sometimes congenital and might be associated with malformations. On the other hand it might be secondary to haemorrhage into the arachnoid, wasting of the brain or obliteration of the sinuses by disease. He thought that most cases were due to "a slow kind of inflammation of the arachnoid". In retrospect West seems to have had a remarkably clear conception of the principal causes of hydrocephalus, although the mechanism whereby fluid accumulated in the ventricles was still obscure.

Indeed further progress was hardly possible without an understanding of the physiological anatomy of the third circulation, that is of the cerebro-spinal fluid. The idea that such a circulation existed awaited the fuller investigations of the nineteenth century anatomists. The discovery by Magendie in 1825 of the foramen that bears his name was followed by a confirmatory description of it by Luschka in 1859, who also described the two lateral openings in the fourth ventricle. It is of interest that Luschka appeared to attach greater importance to the foramen of Magendie, as he named it, than to the lateral foramina. Yet up to our time it is the foramen of Magendie whose existence has been the most debated. Perhaps the fact that it is known to be absent in the horse, pig and possibly other mammals, has encouraged the belief that it is no more than an artefact. In the nineteenth century there was certainly strong opposition to the idea that any of these foramina existed, and the opinion of authorities such as Reichert and Kölliker in this sense doubtless carried great weight. The highest tribute is therefore due to the Swedish workers, Key and Retzius, who in 1875 published a beautifully illustrated study of the anatomy of the nervous system, paying special attention to the meninges and the cerebro-spinal pathway. They reaffirmed the existence of the foramina of Magendie and Luschka, and gave detailed descriptions of their morphology, derived both by dissection and by injection experiments.

In this country strong support in the same direction had already been given by the famous group of teachers at Guy's Hospital. Foremost amongst these was John Hilton who, in his classical lectures on "Rest and Pain", first published in 1863, described and figured the foramen of Magendie in normal

subjects. "The existence of this cerebro-spinal aperture underneath the cerebellum, and between the cerebellum and the medulla oblongata, is not perhaps universally admitted; but I believe, beyond all doubt, that it is the normal arrangement of structure that there should be such an aperture." He adds that, in researches dating back to 1844, he had been at pains to verify its existence and had failed to find it in only one instance: in this case there was an abnormal accumulation of fluid in the interior of the brain. He concluded that the hydrocephalus was due to the occlusion of the foramen.

In his Croonian lectures in 1881 on the influence of the circulation on the nervous system, Moxon redescribed the foramen of Magendie on the basis of an examination of upwards of 70 brains, including foetal specimens. He reproached both the anatomists and surgeons for their neglect of the anatomy of the fourth ventricle. "Not long ago", he says, "a Guy's student was seriously reprehended by an examiner of the Royal College of Surgeons for speaking of a choroid plexus in the fourth ventricle. He was informed that he ought to know that the choroid plexuses are in the lateral ventricles." Yet there is still much to be learnt about the anatomical vagaries of this region—for instance, the variable extension upon the surface of the inferior vermis of the choroid plexus from the foramen of Magendie where it may, to quote

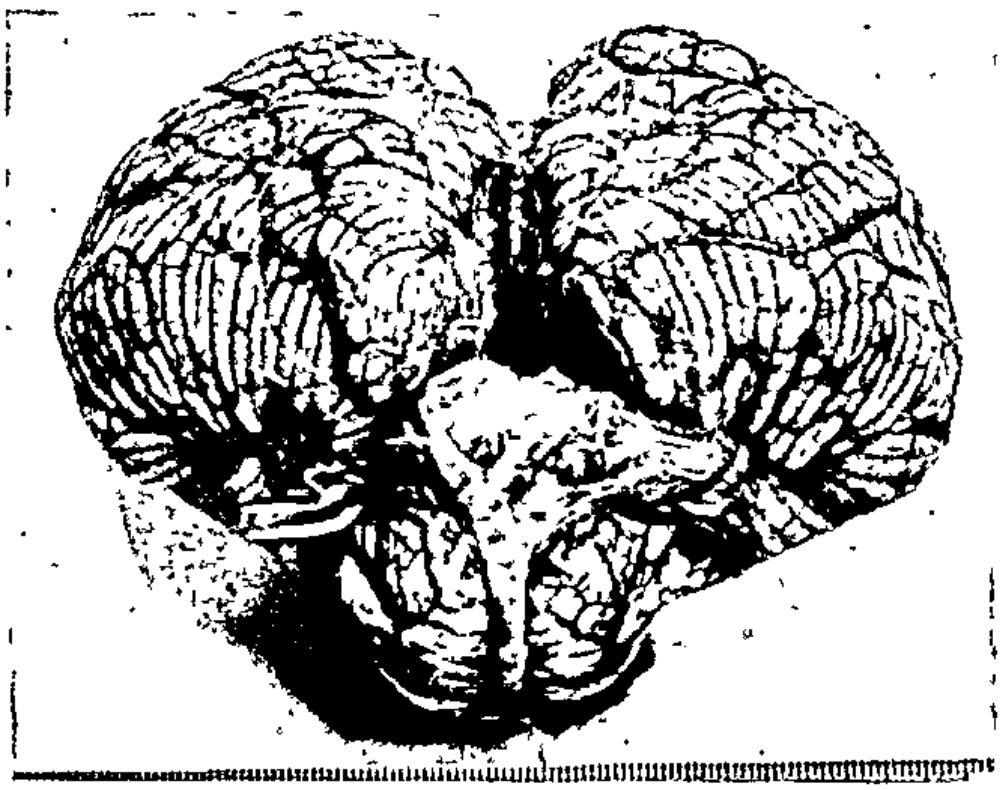


FIG 1: The parallel dark streaks over the inferior vermis represent choroid plexus

Moxon again, "wander out nearly an inch into the subarachnoid space in the most regardless manner" (Fig. 1). This anatomical feature, easily verified in the postmortem room, might in itself seem good evidence of the existence of the foramen with which it stands in relation. Nevertheless the controversy has continued into the present century. Thus Bland-Sutton wrote in 1923: "This

foramen has had such a charm for teachers that it maintains a place in textbooks although sealed up by practical anatomists many years ago". To which Wood Jones (1923) replied: "As a teacher I fully admit the charm of this foramen, and as a practical anatomist I also regard it with affection, for of its presence in the undisturbed condition of the roof plate I have no doubt whatever". The confidence displayed by Wood Jones is shared in present times by the neurosurgeons who so frequently expose this part of the brain at operation, and note both the size and shape of the foramen as well as the passage of fluid through its lumen. The controversy may therefore be regarded as having passed into history.

The anatomical discoveries of the nineteenth century had, however, in the meantime paved the way for progress in our knowledge of the circulation of the cerebro-spinal fluid. The work of Key and Retzius was followed many years later by that of Lewis Weed (1917), whose researches upon the embryological development of the cerebro-spinal spaces in the pig and man are of fundamental importance. Weed correlated the first appearance of villous tufts upon the choroid plexuses with the extraventricular spread of cerebro-spinal fluid into the tissues posterior to the rhombic roof. Hence an opening up of a series of spaces in the foetal mesenchyme could be traced, with the formation of the cisterns and the minuter subarachnoid spaces that characterize the cerebral leptomeninges, progressing at length to the convexities of the brain.

Further evidence exists to show that the cerebro-spinal fluid is actually formed by the choroid plexuses, though the precise nature of the mechanism has not yet been established. This evidence is merely summarized here. The observation by Harvey Cushing (1914), in several cases, of the formation of drops of clear fluid upon the surface of the plexus when exploring the lateral ventricle at operation was corroborated by Howe (1929) who saw a similar "sweating" of the plexus by direct examination with a stereoscopic microscope in experimental animals. Schaltenbrand and Putnam (1927) injected fluorescein intravenously into animals and observed the formation of greenish fluid on the choroid plexuses. Dandy (1919) showed that occlusion of the foramen of Monro led to the distension of the corresponding ventricle when the choroid plexus was intact; if the plexus was simultaneously removed no distension occurred. Putnam (1934) applied this knowledge when he introduced the operation of coagulation of the plexuses in the lateral ventricles for the relief of hydrocephalus. It has legitimately been argued that artificial conditions are introduced in all these observations and experiments, but such arguments have on the whole carried little weight except amongst the minority who oppose the theory that the plexuses are the site of formation of the cerebro-spinal fluid, and hold that they act rather as an absorbing apparatus (Askanazy, 1914; Klestadt, 1915; Hassin, 1930 b). The presence of iron-pigment granules in the choroidal epithelium following intraventricular haemorrhage, and of carmine following the injection of this dye into a lateral ventricle, has been used as evidence in support of this alternative theory. The state of atrophy of the plexuses in advanced stages of internal hydrocephalus has also been advanced as evidence in this sense. But the same criticism as before may be brought to bear on these observations: namely, that the conditions imposed upon the brain are abnormal. Moreover Wislocki and Putnam (1921), on injecting colloidal dyes into the ventricles, found some evidence of absorption on the part of the ependyma, but none attributable to the choroid plexus. It is indeed true that granules of iron pigment may frequently be found in the

choroidal epithelium in cases where intraventricular haemorrhage has previously occurred. While this may reasonably be regarded as evidence of absorptive activity it by no means precludes concomitant secretory activity. For this the renal epithelium provides a physiological parallel.

From the experimental evidence, then, the majority of observers are of the opinion that the choroid plexuses are responsible for the greater part of the cerebro-spinal fluid.

Knowledge concerning the absorption of the cerebro-spinal fluid is even less complete. Leaving on one side the minority view that favours the choroid plexus with this function, it appears that the bulk of evidence points to absorption through the arachnoid villi. For the earliest conception of this theory it is necessary to go back to Key and Retzius (1875). By injection experiments they traced the cerebro-spinal pathway to the Pacchionian bodies, in the cells of which the injected dye became deposited. They believed in the existence of stomata between these endothelial cells whereby fluid passed from the subarachnoid into the subdural space and thence into the venous sinuses. Their theory was widely accepted until it was recognized that the Pacchionian bodies are restricted to adults, and are absent in infancy, and in the anthropoids and lower mammals. In 1913 Dandy and Blackfan published the results of experiments in which phenol-sulphone-phthalein was injected into the cerebro-spinal pathway: from these they formed the opinion that absorption of the fluid took place diffusely through the veins of the subarachnoid space. They adduced no evidence, however, which was incompatible with Weed's theory, published a year later, that the arachnoid villi are responsible for absorption. These villi resemble the Pacchionian bodies on a microscopic scale and bear a similar relation to the great venous sinuses. They are present in infancy and in the lower mammals. Weed was of the opinion that the fluid passed through the cells of the arachnoid villi to enter the venous blood-stream and not through intercellular stomata. Dandy's later estimate (1921 a) that 1/4 to 1/5 of the cerebro-spinal fluid is absorbed from the spinal subarachnoid space and the remainder from the surface of the brain agrees well with what is known of the distribution of the arachnoid villi. Thus by far the greater number of these structures are to be found within the cranial cavity; their occurrence in relation to the spinal nerve-roots has been described by Hassin (1930a). An accessory route of absorption for the cerebro-spinal fluid is provided by certain parts of the lymphatic system. Thus Key and Retzius were able to inject the cervical lymphatics from the spinal subarachnoid space and this has been confirmed by subsequent workers. Weed, using the Prussian-blue technique, demonstrated the passage of cerebro-spinal fluid by way of the cranial nerves to the cervical lymphatics. It is improbable, however, that more than small amounts of fluid travel by this route.

Now with regard to the pathogenesis of internal hydrocephalus it is theoretically arguable that an excess of cerebro-spinal fluid within the ventricles might arise in one of three main ways: first, through over-secretion from the plexuses; secondly, through the interposition of an obstruction at some point in the cerebro-spinal pathway; or, thirdly from impairment of absorption. These possibilities must now be examined.

Hydrocephalus from over-secretion of cerebro-spinal fluid has been claimed in association with two distinct pathological conditions. The first of these is a diffuse hypertrophy of the choroid plexuses of the lateral ventricles. Two such cases are on record (Claisse and Levy, 1897; Loyal Davis, 1924). A

section of the brain in Loyal Davis' case (Fig. 2) shows the symmetrical enlargement of the ventricles in a child of fifteen months and the enlarged, richly villous plexuses. Histologically these showed merely an accentuation of their normal structure. But in Davis' most interesting report there is no mention of the microscopical appearances of the basal leptomeninges, and

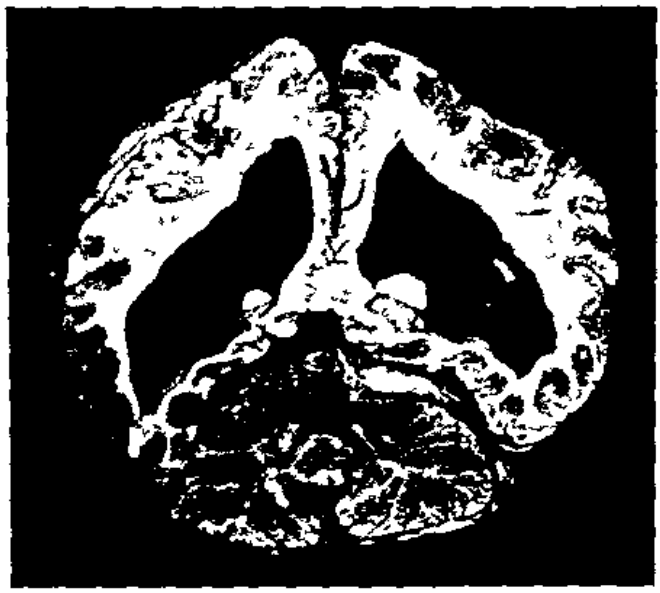


FIG. 2: *Section through brain to show bilateral hypertrophy of choroid plexus (by kind permission of Dr. Loyal Davis)*

hence chronic meningitis was not specifically excluded; exclusion of that condition was desirable because there was a history of trauma to the head a few days before the onset of symptoms. The only other case of this kind on record, that of Claisse and Levy, was also in an infant and again meningitis was not excluded in the description. Hence this cause of hydrocephalus is provisionally regarded here as non-proven*. Should this reservation in the acceptance of these two cases at their face-value be considered unjustified, the reader is referred to Case 40 (p. 75). In this case, in an infant of eighteen weeks, the hydrocephalus was undoubtedly due to a chronic, low-grade meningitis of unknown ætiology, though little was visible to the naked eye. The choroid plexus of the right lateral ventricle bore a large papilloma to which, in the absence of any other explanation, the hydrocephalus might have been attributed (Fig. 49, p. 76).

Over-secretion of cerebro-spinal fluid, with consequent hydrocephalus, has also been postulated following thrombosis of the great vein of Galen. It is supposed that such thrombosis produces an excessive secretion of fluid through venous congestion in the plexuses. This idea was current in the last century and underwent a vigorous revival following the experiments of Dandy and Blackfan (1914) and of Guleke (1930), in which it was claimed that occlusion of the vein of Galen in dogs resulted in hydrocephalus. Their results however have not been confirmed (Bedford, 1934; Schlesinger, 1940), and this theory is now usually discredited. It is of interest that, according to Bedford (*loc. cit.*) no undisputed cases of this kind in human subjects have been recorded. None occurs in the present series. One case, however, illustrates the need for cautious interpretation. The main details of this are as follows:

K.G., a male infant aged six months (Reg. No. 14290/1934). Birth was at full-term, the labour being normal. The child remained well until the fifth day when convulsions began.

* See appendix.

Enlargement of the head was first noticed at three weeks, and it steadily increased. Ventricular puncture, at the age of two months, yielded faintly yellow fluid under a pressure of 100 mm. containing 1 per cent. of protein and 220 cells per c.mm., of which 70 per cent. were lymphocytes and 28 per cent. neutrophil leucocytes. Indigo-carmine was injected into the lateral ventricles on several occasions but did not appear in the lumbar fluid. The latter was colourless and contained 0·08 per cent. of protein and 11 cells per c.mm., all lymphocytes.

At *necropsy* (P.M. 188/1935) the head measured 50 cm. in circumference. The lateral and third ventricles were greatly enlarged, while the fourth ventricle was of normal size. Both frontal and occipital poles of the cerebral hemispheres presented the appearances of microgyria; the tissue here was unusually firm and, on section, there was conspicuous orange and yellow pigmentation of the narrowed subcortical white matter, with pinhead areas of cavitation in the pigmented areas. The ependyma was converted into a tough glistening grey membrane, stained in places a faint yellowish-brown. The choroid plexuses were buried in similar grey tissue. Transverse section through the mid-brain revealed an aqueduct of pin-point dimensions surrounded by a dense milky-white zone suggestive of gliosis. There was orange-brown pigmentation of the tissues about the great vein of Galen.

Microscopic examination revealed recanalization of organized thrombus filling the vein of Galen. The ependyma of the lateral ventricles was replaced by dense collagenous tissue, the deeper layers of which were profusely infiltrated with small lymphocytes, plasma cells, and large mononuclear cells laden with iron pigment. The choroid plexuses were embedded in similar tissue. In the fourth ventricle the ependyma was raised into granulations over the floor, and was coated in places with flocculent cellular debris containing large mononuclear cells, some of which contained iron pigment. The aqueduct was subdivided into a considerable number of irregularly-shaped, ependymal channels of which the two largest occupied the median raphe, one above the other, and were partly blocked with debris and cellular infiltration. The surrounding tissue showed moderate gliosis and infiltration with a few plasma cells, leucocytes and an occasional large mononuclear cell containing pigment.

The aqueduct thus displayed a congenital malformation of a kind that will be considered at greater length elsewhere (p. 14); it is usually associated with gross hydrocephalus but, as will be shown, is compatible with survival to adult life with little or no hydrocephalus in some cases. The inflammatory changes present throughout the ependyma, and particularly in the lateral ventricles, were of the chronic, low-grade character that follows haemorrhage and necrosis. They were interpreted, therefore, as the result of venous infarction following thrombotic occlusion of the vein of Galen. There is evidence, from the examination of early examples complicating birth-injury, that the principal effect of such thrombosis upon the brain is an extensive, but uneven, haemorrhagic infarction of the area drained by the Galenic system of veins; thus the ependyma of the lateral ventricles is extensively destroyed. While this, in itself, could not be expected to produce internal hydrocephalus, the shedding of cellular debris into the ventricular cavity and the resulting inflammatory reaction might well produce such an effect indirectly, either by blocking the aqueduct or by setting up a low-grade inflammation in the basal leptomeninges. In the present case the carriage of debris into a malformed aqueduct, as described, may well have precipitated the onset of the hydrocephalus. The history agrees with this interpretation: in particular the failure of dye to reach the lumbar fluid from the ventricles, and the different composition of the samples of fluid obtained from the ventricles and lumbar region indicate an effective block within the ventricular system.

The second possible mechanism through which hydrocephalus may arise must now be considered, namely, the interposition of some obstruction in the cerebro-spinal pathway. Study of the series of cases presented in this report suggests that this is responsible for at least 99 per cent. of all cases of internal hydrocephalus. A consideration of the anatomy of the pathway shows that there are certain narrowings, such as the various foramina, the aqueduct of Sylvius, and the leptomeningeal spaces at the level of the tentorial opening, where the development of various pathological processes might be expected

to obstruct the free passage of fluid. These expectations are fully realized in the course of experience. While the character of the lesions is varied the general rule holds that, wherever they arise, dilatation of the pathway proceeds in a retrograde fashion to the lateral ventricles. And in practice this rule forms a useful guide in searching for the responsible lesion should this not at first be obvious. Clinically also there is a useful test, elaborated by Dandy and Blackfan (1913) which led them to distinguish between "communicating" and "non-communicating" types of hydrocephalus. Thus when phenol-sulphonephthalein is injected into a lateral ventricle it should normally be recovered from the spinal fluid in from two to three minutes, and from the urine in from ten to twelve minutes. If, in a hydrocephalic subject, the dye is not recovered from the spinal fluid, or is greatly delayed in transit, the hydrocephalus is said to be of the non-communicating type. This means that the ventricular system is sealed off at some level which may be as far caudal as the fourth ventricle foramina. If the dye appears in the spinal fluid in the normal time, but its excretion in the urine is greatly delayed, the hydrocephalus is of the communicating type: the obstruction then lies in the meninges distal to the fourth ventricle foramina and thus impedes absorption. Alternatively there might be some impairment of the absorbing apparatus: for example, blockage or maldevelopment of the arachnoid villi.

This introduces the third possible mechanism in the production of hydrocephalus. If the thesis that the cerebro-spinal fluid normally drains by the arachnoid villi into the blood-stream is accepted, then alteration of these villi by disease might be expected to result in a damming back of fluid and ultimately in some degree of internal hydrocephalus. This question, which must be discussed more fully later (pp. 86–94) is highly controversial; it will suffice here to observe that there is some support for the view that sinus thrombosis is followed, in appropriate circumstances, by appreciable internal hydrocephalus.

Finally, how should cases of internal hydrocephalus be classified for purposes of description? The separation into communicating and non-communicating groups is useful clinically for diagnostic and therapeutic purposes, but not so serviceable in pathology. In the textbooks, hydrocephalus is discussed under the headings of "congenital" and "acquired", "idiopathic" and "secondary" groups; but these divisions, in the light of morbid anatomy, are meaningless. It appears best, therefore, to describe the cases according to the pathological findings. A purely topographical basis might be adopted with the description of lesions to be found at different levels of the cerebro-spinal pathway. Such a regional treatment would, however, lead to much repetition. The least objectionable solution appears to lie in basing the description of the cases upon the main, time-honoured categories of pathological lesions. In what follows, therefore, the cases will be grouped under the headings of malformations, inflammations, tumours, and so forth.

Chapter II

MALDEVELOPMENTS

Developmental errors are a frequent cause of internal hydrocephalus. The subjects in which they arise are often stillborn because the size of the head is incompatible with normal delivery; in others the hydrocephalus may become apparent shortly after birth. But occasionally the abnormality is not of sufficient magnitude to produce neurological symptoms. The developmental errors responsible for hydrocephalus are usually demonstrable at one of the anatomical points at which the cerebro-spinal pathway is normally constricted: the foramina of Monro, the aqueduct of Sylvius, or the fourth ventricle foramina.

It follows that most of the cases clinically recognized as "congenital hydrocephalus" are included in this group. The ætiological factors concerned in such forms of hydrocephalus are obscure. In some cases an inflammatory origin cannot be excluded, but no evidence has been found in the present series—or indeed in any case recorded in the Bernhard Baron Institute since 1907—that syphilis is responsible. This form of infection is specially mentioned because it has often been quoted as the commonest cause of congenital hydrocephalus. But the evidence provided by the present series points to maldevelopment as the usual cause. Those described in this section rest probably upon a genetic basis, though the demonstration of hereditary factors is obviously difficult in the human species. In the mouse, however, Grüneberg (1943 a) recognizes three forms of inherited hydrocephalus, two at least of which may profitably be compared with those occurring in man. The first of these was identified by Clark (1933-1934) and shown to be transmitted as a simple Mendelian recessive. The hydrocephalus appeared at birth or a week or two later, and proved fatal in the third or fourth week of post-natal life. Histological examination of serial sections revealed extreme narrowing of the aqueduct, apparently a true stenosis, and the fourth ventricle was of normal size. The second form of hereditary hydrocephalus was described by Zimmermann (1933) in Berlin. Although its anatomical basis has not been demonstrated, it has been proved by breeding experiments to be genetically distinct from Clark's variety (Clark, 1935). In a third genetically distinct form (Grüneberg, 1943 b), due to a recessive gene, the hydrocephalus appears to be caused by retardation of the growth of cartilage at the base of the skull, which leads to compression of the hind-brain and obstruction to the passage of cerebro-spinal fluid. This condition is reminiscent of achondroplasia in man, an hereditary disease associated with hydrocephalus (see p. 39).

In man it is of interest that spina bifida, a condition frequently associated with hydrocephalus, may be familial (Butler-Smythe, 1889; Pybus, 1921), and has been observed in binovular twins (Fry, 1943). In a series of 546 cases recently reported from the Children's Hospital, Boston by Ingraham and Swan (1943), the familial incidence was quoted as 6 per cent.

Obstruction at the foramen of Monro leads to dilatation of the corresponding lateral ventricle. No instance of such obstruction due to maldevelopment appears in the present series of cases, but a few have been recorded elsewhere; in none, however, is it certain that an inflammatory origin can be excluded. Spiller (1902) reported a case in a feeble-minded boy of 14 years who developed progressive difficulty in walking, accompanied by contractures of the left upper

and lower limbs. The right lateral ventricle was intensely dilated, the cerebral tissues being reduced in places to a membrane 1/8 inch (0·3 cm.) thick. The corresponding foramen of Monro was occupied by a nodule which projected from its external wall. Microscopically this nodule was described as "composed of tissue like that of brain substance, although its structure resembled also fibrous tissue". At one part it "was bordered by cells with round nuclei several layers deep, and these were evidently derived from the ependymal lining". Although Spiller entertained the view that this lesion might have been of tuberculous origin in consideration of the fact that one of the suprarenals was tuberculous, there is nothing in the description, apart from a focal thickening (of doubtful significance) of the choroid plexus, to support this diagnosis, and it seems more probable that the nodule was an ependymal polyp of the kind described below (p. 50).

Dott (1927) operated successfully upon a female infant of 9 months in whom gross dilatation of the left lateral ventricle was due to obliteration of the foramen of Monro. He made an opening in the septum pellucidum, and an excised portion showed, on microscopical examination, extreme gliosis. The ependyma on the left side had been destroyed; that on the right side was normal. The age of the patient in this case strongly suggests a developmental basis for the lesion. There is no record of any inflammatory cellular exudate, and the presence of gliosis cannot be claimed as proof of inflammation, since this would certainly be evoked in the subependymal tissues by distension of the ventricle and destruction of the ependymal epithelium (see p. 122).

Again, Tinel, de Martel and Guillaume (1932), in operating upon a child of 10 years with a greatly dilated right ventricle, found the ependyma to be grey and thickened while the septum pellucidum was thin and contained, near its centre, a perforation 1 cm. in diameter. The right foramen of Monro was occluded by a membranous feltwork ("feutrage"). Although the authors considered their case to be similar to that described by Dott, the absence of microscopical examination leaves the matter in doubt.

Aqueduct of Sylvius

This is a site of the first importance in considering maldevelopment as a cause of hydrocephalus. Malformation of the aqueduct is a common lesion in congenital hydrocephalus and may take the form either of a simple stenosis or the condition commonly known as "atresia".

STENOSIS

This is here defined for convenience as a state in which the aqueduct is histologically normal but abnormally small. It is distinguished from gliosis of the aqueduct (see p. 41) by the absence of any increase in the subependymal glia. Little is known of this condition; moreover we have no precise data concerning the normal variations in the calibre of the lumen. It is common knowledge that the outline of the lumen in cross-section alters at different points of its course (Quain, 1909), but the text-book descriptions appear to date back to Gerlach (1858) who prepared sections from material hardened in bichromate, and drew, with a camera lucida, every third or fourth section in the 120 cut from each specimen. The results, magnified ten times, are reproduced as 38 outline drawings on three Plates and a selection of nine of these is reproduced in Fig. 3. From this it will be seen that, proceeding caudally, the lumen narrows towards the centre of the anterior corpora quadrigemina, then widens.

and narrows again as the posterior corpora quadrigemina are approached and finally expands into the fourth ventricle. Thus observations made on potential examples of stenosis should take these variations into account and suitable control sections should be available for comparison. In a more recent study of the anatomy of the aqueduct Turkewitsch (1936) gives two-plane measurements of the lumen at different levels, but these are referable to points in the internal anatomy of the aqueduct and not to its surface anatomy. His descriptions of the shape of the lumen do not agree either with Gerlach's or with those of current textbooks. The latter, however, appear to be derived from Gerlach's drawings though their source is seldom indicated.

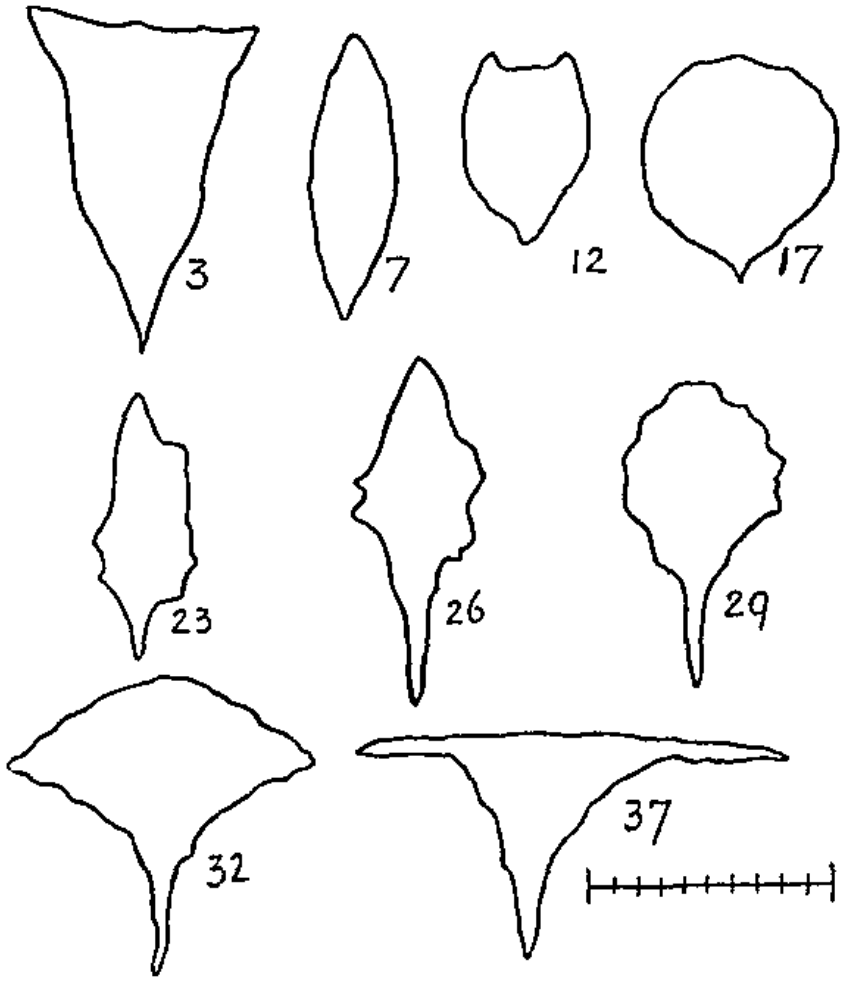


FIG. 3. Tracings of aqueduct in transverse section at different levels, taken from Gerlach (1858). × 10. 3, posterior commissure; 7, anterior A.C.Q.; 12, middle A.C.Q.; 17, posterior A.C.Q.; 23, between A.C.Q. and P.C.Q.; 26, anterior P.C.Q.; 29, posterior P.C.Q.; 32, hind end P.C.Q.; 37, opening into 4th ventricle

As matters stand, therefore, we do not know either the normal range of variation in the calibre of the aqueduct, nor what margin this provides beyond what is essential for the adequate conduction of cerebro-spinal fluid from the third to the fourth ventricle. But when the relatively voluminous aqueduct of some of the lower vertebrates, such as the rabbit, is compared with the human it may be fair to surmise that the working margin is probably slight.

Both from a survey of the literature and from personal experience it seems that simple stenosis of the aqueduct is a rare condition. A case was reported by Spiller and Allen (1907) in a woman, said to have been hydrocephalic from

birth, who lived to the age of 62. She was epileptic and had occasional attacks of vomiting and vertigo from no obvious cause. Her mentality was good. *On examination of the brain, the lateral and third ventricles were grossly* dilated and the aqueduct was hardly larger than the point of a pin. Microscopical examination showed that the ependymal lining was intact. The lesion was interpreted as a congenital malformation.

The present series of cases provides two examples:

Case 1: A male, aged 39 (P.M. 272/1937; Reg. No. 11694 Surg). Death was due to an unrelated intercurrent affection. No neurological abnormality was suspected and no relevant clinical features were noted. At necropsy a considerable degree of internal hydrocephalus was disclosed, involving the third and lateral ventricles. The foramina of Monro measured 0 6 cm. in diameter, and the grey commissure was 0 8 cm. long. The only explanation found for this hydrocephalus was a constriction of the aqueduct to the size of a pin's head (0 075 cm.) at the level of the posterior corpora quadrigemina. Microscopical examination shows it to be of normal shape and structure, but considerably smaller than a normal control cut at the same level (*Fig.* 4).

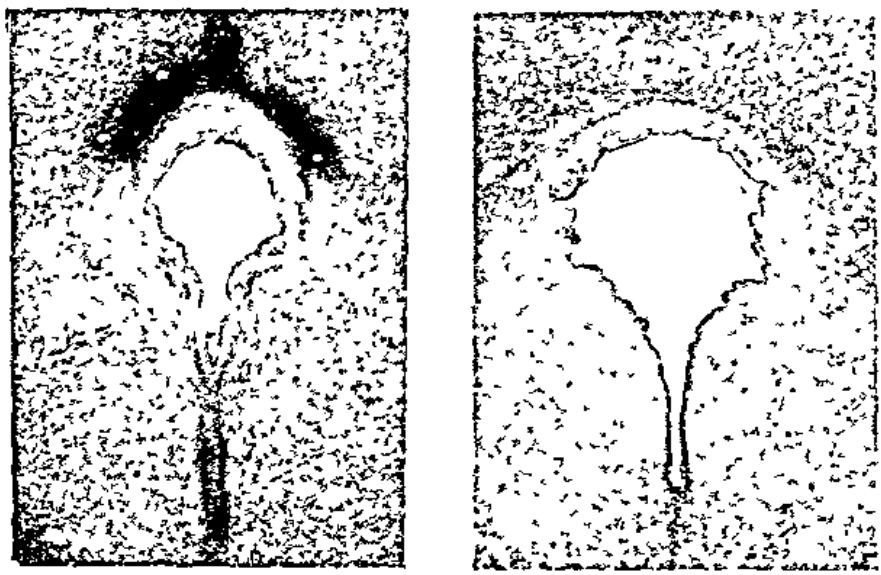


Fig. 4: *Case 1.* Simple stenosis of aqueduct (left) with control at same level of aqueduct (right) H. and E. × 25

Case 2: A stillborn female infant (P.M. 137/1939). Perforation of the brain was necessary to effect delivery. The circumference of the skull when collapsed was about 45 cm. The third and lateral ventricles were grossly dilated. The corpus callosum was extremely thin and no trace was found of the septum pellucidum. The choroid plexuses were greatly atrophied and the ependyma over the basal ganglia was sparsely studded with pinpoint granulations. The medial aspect of both occipital lobes was formed of a translucent membrane, composed of the leptomeninges, extending from the pole to the thinned out splenium of the corpus callosum. The mid-brain was deformed through fusion of each pair of the corpora quadrigemina into a single medial mass. On transverse section the aqueduct beneath each mass was visible as a slit about 0 1 cm long, but between them it was of pinpoint size. The cerebellum also was deformed: it was small, flattened, and composed of the united lateral lobes with no trace of vermis. The foramen of Magendie was present and patent. The leptomeninges appeared normal.

Microscopic examination (*Fig.* 5): The aqueduct is obviously of abnormal shape and greatly reduced in size. There is no gliosis or histological evidence of inflammation in its neighbourhood. The cellularity of the tissue about the dorsal part of the aqueduct, which can be seen in the photographs, is due to displaced ependymal cells. These form occasional tubules or rosettes. This detachment of ependymal cells, and the branching tendency of the lumen, suggest a relationship with the form of abnormality to be described next, in which the appearances are more complex.

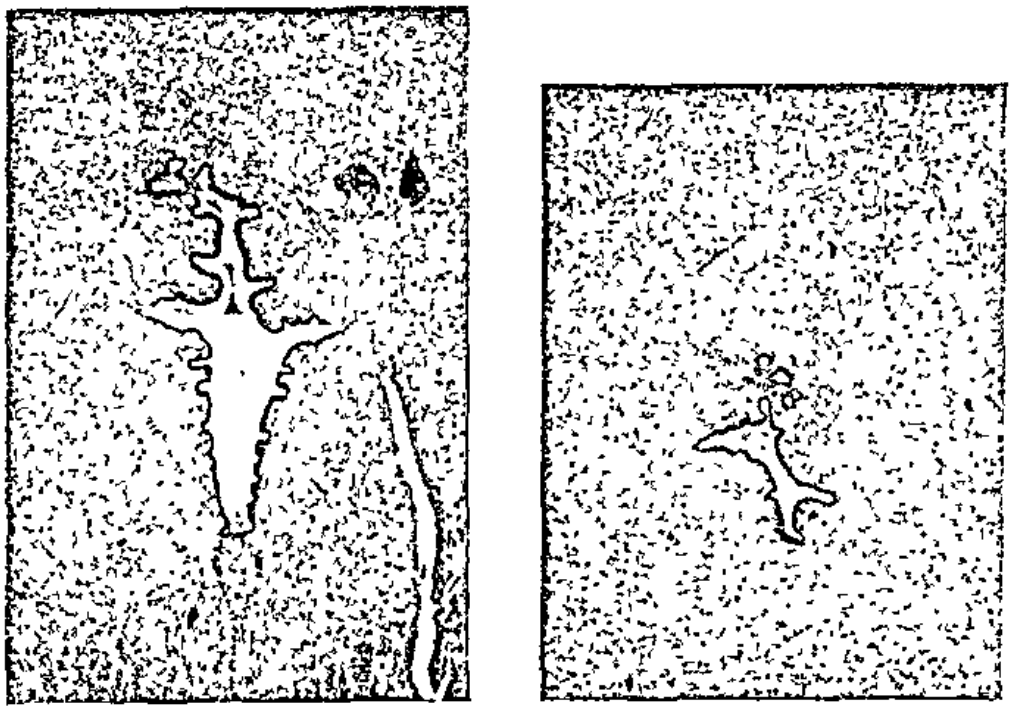


FIG. 5: *Case 2:* Transverse section of aqueduct at two levels ; maximum stenosis on right. H. and E. × 25

FORKING ("ATRESIA") OF THE AQUEDUCT

Cases 3-12

This is a common cause of congenital hydrocephalus. The condition is often described as "atresia". This term implies non-patency and has doubtless been used because the lumen of the aqueduct is often invisible to the naked eye for a variable part of its length. But in serial sections of such material it has proved impossible to find any point at which the lumen has entirely disappeared. "Atresia" is therefore incorrect and the term "forking", which describes the morphological abnormality of the aqueduct, appears preferable. True atresia has not been encountered so far.

In the ten cases of this malformation that were examined microscopically the aqueduct is represented, for part of its course, by two distinct channels situated in the mid-sagittal plane and separated from one another by normal nervous tissue. The channels are lined with an intact, often columnar ependymal epithelium without any excess of gliosis in the immediately adjacent tissue. As shown in the accompanying photomicrograph (Fig. 6) the ventral channel is usually a simple slit in the dorso-ventral plane. The dorsal channel is considerably branched and the neighbouring tissue contains many groups of displaced ependymal cells, many of which form tubules. In one example the dorsal channel formed a wide transverse slit which became subdivided caudally into a row of minute tubules. Serial sections in three cases show that either the dorsal or the ventral channel may unite the ventricles, the other channel dwindling and disappearing either in a cephalic or caudal direction. Other cases, not so fully examined, indicate that in some the two channels become fused at some point in the course of the aqueduct, and thereafter the lumen acquires a more normal aspect.

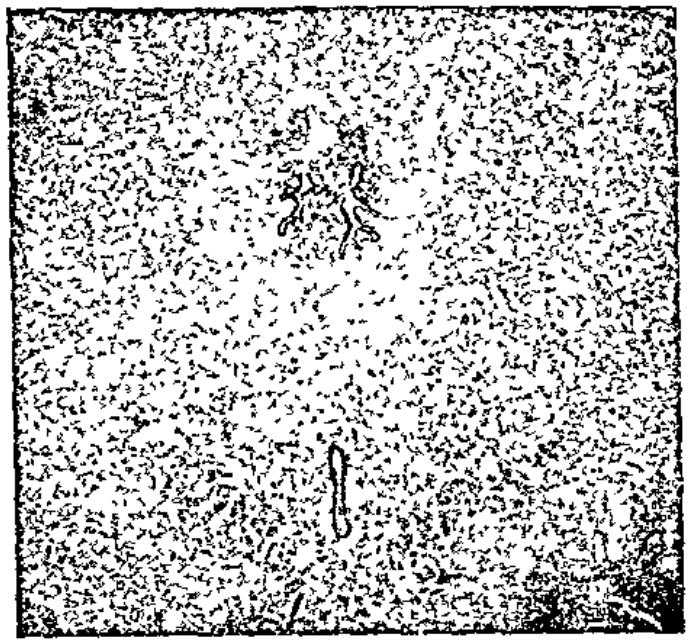


FIG. 6: Forking ("atresia") of aqueduct, showing characteristic sub-division into dorsal and ventral channels. H. and E. × 14·5

Though the aqueduct is thus demonstrably patent it appears inadequate to maintain the circulation of the cerebro-spinal fluid, and hydrocephalus is attributable to this defect. In this connection it is noteworthy that Parker and Kernohan (1933), in a paper on stenosis of the aqueduct, describe and figure a similar condition in a girl of 11 years who had suffered from convulsions for 3 years but was not hydrocephalic. In this case the dorsal part of the aqueduct, as figured, is relatively large—calculations showing that it must have measured 2·5 by 0·4 mm. in cross-section. It may thus have been large enough to form a competent channel. In Case 20 of the present series (p. 34), in which a sacral meningocele was associated with a slight degree of internal hydrocephalus, a similar malformation of the aqueduct was present but the dorsal channel was patent throughout and only slightly reduced in calibre. Moreover the same type of deformity has twice been encountered by chance during the microscopic examination of non-hydrocephalic subjects dying from other causes: in both of these a vestigial ventral channel was associated with a dorsal channel which in all respects resembled the normal aqueduct.

The type of malformation described has been recognized and described in various other papers, but has often been interpreted as the result of ependymitis and gliosis rather than of developmental error (Fraser and Dott, 1922-1923). In the older literature "atresia" was generally held to be a syphilitic lesion, an intra-uterine infection causing secondary glial proliferation. Forking of the aqueduct was, however, accurately described by de Lange (1929) in a case of spina bifida, and regarded by her as a malformation ("Missbildung"). There can be little doubt that great confusion has existed between this so-called "atresia" and "gliosis" of the aqueduct. Thus Roback and Gerstle (1936), describing six cases of congenital atresia and stenosis in young infants, clearly regard the subdivision of the aqueduct as the result of an ingrowth of the subependymal glia to form bridges across what was once a single lumen. Yet they note the absence of inflammatory features from two of the cases and admit the possibility of maldevelopment in discussing four. Whatever the

cause of gliosis with resulting stenosis, deformity and subdivision of the aqueduct (see p. 44) there can be no question that the type of deformity with which we are at present concerned is, in fact, the result of maldevelopment. The reasons for this view may be recapitutated briefly:

(1) There is no excess of gliosis about the malformed portion of aqueduct, nor any inflammatory cellular infiltration.
(2) The dorsal and ventral channels are separated by normal neural tissue.
(3) Associated malformations of the mid-brain are commonly found, such as fusion of the corpora quadrigemina. In one case fusion of the nuclei of the third nerve into a medial mass was observed.
(4) Remoter malformations are common. In the present series of ten cases spina bifida was present in seven instances. In one of these, a case of spina bifida occulta, there was a small dermoid cyst in the vermis, extensive malformations of the ribs and sternum, and a double pelvis and ureter to the right kidney. In an eighth case there was an associated turricephaly, with gross cerebral malformations.

In the six cases reported by Roback and Gerstle spina bifida was present in four, club-foot in one and deformity of the toes in one case.

Ætiology. From the foregoing observations it is concluded that the basis of this forking of the aqueduct lies in a congenital maldevelopment. The cause of this is unknown. There is no evidence that syphilis, or any other infection, plays a part, often as this has been postulated (Marburg, 1940). There is nothing in the histological picture in favour of an inflammatory causation. Spiller (1916) regarded it as due to an exaggerated closing-in of the tissues forming the aqueduct during embryonic development. He compared it with the subdivision, or even obliteration, of the central canal of the spinal cord that is so commonly seen especially in the lower thoracic and lumbar segments. Such an explanation however does not account for the remarkably constant pattern of the malformation as described above, nor for the separation of the dorsal and ventral channels of the aqueduct by normal neural tissue. Spiller's theory seems more applicable to "gliosis" of the aqueduct (see p. 47) and might be advanced to explain a stenosis such as occurred in Case 2. In view of the frequency with which these malformations of the aqueduct are associated with spina bifida it may be mentioned that Lichtenstein (1942) regards stenosis of the aqueduct as the result of caudal traction upon the brain-stem in this condition. This view will be discussed in the section upon spina bifida and the associated deformities of the nervous system. No support for his theory is provided by the present series of cases.

SEPTUM FORMATION

In the two cases to be described the hind part of the aqueduct was crossed by a neuroglial septum.

Case 13: Male, 8 years (Maida Vale Hospital) His head had always been rather large. Neurological symptoms dated back for 5 years, when it was first observed that he walked with difficulty and dragged his right leg He frequently complained of headache. A few months before admission to hospital he developed symptoms and signs referable to a lesion of the spinal cord, which was disclosed at operation (Sir Hugh Cairns) to be syringomyelia. At this time hydrocephalic enlargement of the skull was observed, with secondary optic atrophy. He died a year later in a fever hospital during an attack of chicken-pox.

The brain, when examined after fixation, showed great internal hydrocephalus. The foramina of Monro measured 2·5 × 1·3 cm. and the cerebral substance varied in thickness from 0 8 to 3 cm. over the convexities. The proximal end of the aqueduct measured 0 7 cm. in diameter and tapered towards an oblique imperforate septum (Fig. 7) of translucent grey tissue directed ventrally and caudally towards the entrance to the fourth ventricle. Transmitted

light showed the upper third of the septum to be exceedingly thin, and pouched towards the fourth ventricle which was not dilated. There was no evidence of meningitis. In addition there was a papilloma of the choroid plexus measuring 5 cm. in diameter in the vestibule of the left lateral ventricle. The ependyma of the ventricular system was studded with pinpoint and pinhead granulations.

Microscopic examination: The septum is composed of loose-textured fibrillary neuroglia coated in a few places with groups of ependymal cells. Many small islands of displaced ependymal cells were identified in the adjacent tissue above and below the aqueduct. There is no inflammatory cellular infiltration. In the floor of the aqueduct just anterior to the septum is a short, branched diverticulum lined with ependymal cells. No evidence of inflammation was found in sections through a group of ependymal granulations in the right ventricle.

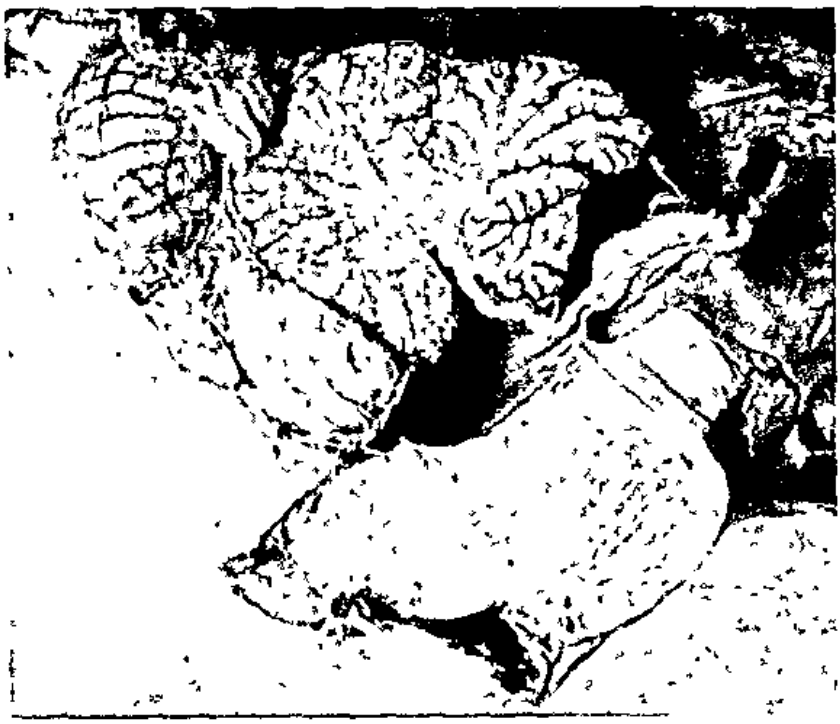


FIG. 7: *Case 13:* An oblique septum of neuroglial tissue traverses the hind end of the aqueduct

Case 14: Male, aged 20 years (Maida Vale Hospital). The following clinical summary is given by kind permission of Dr. Wilfred Harris.

Birth was normal. Enlargement of the head was noticed up to the age of 3½ years, but after that there was no increase. He was somewhat backward at school. At the age of 15–16 he was operated upon for appendicitis after which he became bedridden, and lost the use of his arms and legs. Seven months before death he complained of frontal headaches which became almost continuous. He vomited occasionally. On examination he presented the appearance of gross hydrocephalus and his mental powers were poor. Neurological examination revealed inequality of the pupils, the left being larger than the right, and slight weakness of the left lower face. There was weakness of the right sterno-mastoid and trapezius muscles, and wasting of the muscles of all limbs, especially on the right. Increased tendon reflexes and an extensor plantar response were obtained on both sides. There was no sensory loss. The Wassermann reaction was negative both in blood and cerebro-spinal fluid, which was normal on analysis.

The brain, when examined after fixation, showed great expansion of the cerebral hemispheres. On medial sagittal section the aqueduct was found to be divided by an exceedingly tenuous partition of grey glistening tissue at the proximal end of the otherwise normal fourth ventricle (Fig. 8). With transmitted light a minute perforation was observed at its centre through which a human hair (but not a horse hair) could be passed. Above the septum the aqueduct was slightly dilated (up to 0·3 cm. in diameter). The third and lateral ventricles were grossly dilated, the cerebral substance being from 0·5 to 1·3 cm. thick over the convexities. The ependyma appeared everywhere normal.

Microscopic examination: The tissue composing the septum was unfortunately lost in the preparation of sections. The adjacent tissues showed no histological abnormalities on examination.

FIG. 8. *Case 14:* A thin septum divides the aqueduct transversely at its junction with the fourth ventricle

The appearances of these septa in the aqueduct, combined with a history dating back to early infancy, suggest that they were due to a congenital maldevelopment. The combination of a septum with syringomyelia and a papilloma of the choroid plexus in Case 13 lends support to this view. There was no evidence of inflammation on microscopical examination. The literature throws little light upon the question of their ætiology. A few cases have been reported in which a septum, disclosed at necropsy, was the cause of hydrocephalus. Versé (1915) described the case of a child aged 8¾ years in which the head had been enlarged since early childhood. A thin membrane blocked the opening of the aqueduct and the adjacent ependyma bore small warty granulations. Microscopically there was subependymal glial proliferation and perivascular cellular infiltration in this region. Versé concluded that these indicated a chronic encephalitis though he was unable to find any further changes in the brain substance or meninges. The Wassermann reaction was negative in blood and cerebro-spinal fluid. In Orton's case (1908) the patient survived to the age of 46 years, displaying poor mentality and enlargement of the head. At necropsy a partition, such as was described in Case 13, was found. Microscopical examination showed that small ependymal canaliculi provided routes by which the cerebro-spinal fluid could trickle past the obstruction. This example too was regarded as of inflammatory origin. Doubtless inflammation is capable of exciting the formation of these membranes. Thus in connection with cysticercosis of the brain Versé described another instance in which the cavity of the fourth ventricle was transversely divided by a membrane which lay at the caudal pole of a parasitic cyst. There was gross internal hydrocephalus. The membrane in this case may of course have been coincidental; on the other hand it is well known that these cysts may, when held up and undergoing decay in the fourth ventricle, excite a chronic ependymitis.

Finally, in the interesting case described by Rowbotham (1938), in a girl of 11 years, the hind end of the aqueduct was occluded by a partition, the centre of which was perforated. This lay immediately caudal to an aneurysm (believed to have arisen on one of the perforating branches of the superior cerebellar artery) which was the size of a small pea and bulged into the lumen of the aqueduct. This aneurysm was probably of congenital origin, and the formation of the septum is unexplained unless it also was a developmental error. Rowbotham's case introduces a further type of congenital defect in this region that may cause hydrocephalus. A similar case was recorded by de Lange (1929) in which the aqueduct at the level of the posterior corpora quadrigemina was deformed by a venous aneurysm. Arteriovenous aneurysms, or hamartomata, may arise in this neighbourhood with similar effects, but it is more convenient to consider these in connection with neoplasms in general (see p. 102).

Septum at Site of Foramen of Magendie

The occurrence of neuroglial septa in the aqueduct has been considered, and, while these formations may in some cases have an inflammatory origin, there is little doubt that others are congenital maldevelopments. The same is true of similar structures of a membranous nature occluding the hind end of the fourth ventricle, at the site of the foramen of Magendie. Unfortunately observations limited to macroscopic data outnumber those in which more precise microscopic information is also available, and the literature contains few examples in which a developmental basis can be fairly claimed. The condition moreover appears to be rare. Thus Taggart and Walker (1942) could find references to only eight examples, of which two were operative observations. They omitted the historical case described by John Hilton (1863). In none was there clear evidence to show whether the membrane was an inflammatory product or a congenital abnormality. They reported three new cases, in two of which careful histological examination established without doubt the congenital nature of the abnormality. In their third case permission for necropsy was not obtained, but the operative findings and the clinical resemblance between this and the other two cases suggest that it was of the same kind. To these a further example can be added. It shows much in common with the cases of Taggart and Walker; also a few differences.

Case 15: M.F., a female infant, aged 1 year 1 month (Reg. Nos. 41019, 41089, 40527/1929 and 40149/1930). She was first admitted to the London Hospital six weeks after birth, with moderate hydrocephalus. Birth had been normal at full term. Eight other children in the family were alive and well. On examination the circumference of the head was 40 cm., all sutures were separated and the anterior fontanelle was bulging. There was no appreciation of light or of moving objects. The right retina was detached at the macula; both discs were pale and the retinae streaked with pigment. Lumbar puncture yielded fluid that was cloudy; it contained 410 mg. of protein per 100 c.c., and 155 white cells per c.mm. of which 25 per cent. were neutrophil leucocytes, 65 per cent. lymphocytes and 10 per cent. of endothelial type. Cultures were sterile and no tubercle bacilli were found. The Wassermann reaction was negative. The ventricles were needled three weeks after admission and, at a depth of from 1 to 2 cm., clear yellow fluid was obtained which contained 2 per cent. of protein, 19 cells per c.mm., of which 11 per cent. were neutrophil leucocytes, 59 per cent. lymphocytes and 30 per cent. endothelial cells. Cultures were sterile. Withdrawal of the fluid was followed by a slight decrease in the size of the skull, but it quickly filled out again.

From this time onwards the ventricles were repeatedly needled, the child being readmitted to hospital for this and for further observation. The head steadily increased in size and, 10 months later, was 57·4 cm. in circumference. At that time coarse lateral nystagmus and secondary optic atrophy were observed. Following tapping of the ventricles, 4 c.c. of indigocarmine were introduced. On the following day the spinal fluid, obtained by lumbar puncture, contained no dye, but puncture of the other lateral ventricle showed that it was still present in the ventricular fluid. The child died one month later.

Necropsy (P.M. 179/1930). No important changes were found apart from those in the brain. Death was due to broncho-pneumonia.

The brain showed extreme hydrocephalus, the substance of the cerebral hemispheres being reduced to transparent membranes except in a few areas over the convexities where it was up to 0·05 cm. thick. Much of this effect was due to the development of systems of false diverticula of the lateral ventricles, probably from the frequent needling of the brain. The fourth ventricle also was dilated, and was closed posteriorly by a membrane which was quite free from the arachnoid mater roofing the cisterna magna. No trace of the foramina of Luschka could be found. A few delicate adhesions united the dura to the arachnoid membrane at the base of the skull and over the spinal cord, especially at the site of lumbar puncture.

Microscopic examination· The hind end of the fourth ventricle, together with the occluding membrane and adjacent structures, was divided in the mid-sagittal plane and the opposing surfaces were embedded in paraffin. In the process the membrane became buckled caudalwards, with approximation of the cerebellum to the dorsal surface of the medulla oblongata. Histologically the membrane consists, as shown in Fig. 9, of a neuroglial sheet which is split along its course into two parallel laminae These laminae become separated towards the centre of the membrane to enclose an abortive cerebellar folium (1) and vascularized connective tissue, probably derived from the leptomeninges. The inner aspect of the membrane, towards the lumen of the ventricle, is clothed in places with ependyma. The outer lamina contains myelinated nerve fibres lying in the plane of the section. At the junction of the membrane with the cerebellum an additional sheet, of great tenuity, is stretched caudally to unite with the pia-arachnoid over the lower part of the medulla oblongata. Unfortunately it has been broken in its middle and as the photograph shows, the lower portion is curled over ventrally. This thinner membrane, which is probably the arachnoid of the cisterna magna, is mainly composed of delicate collagenous tissue ; it bears a thin zone of neuroglia on its inner surface and this again is clothed in places with ependymal cells and, dorsally (2), with a tuft of choroid plexus.

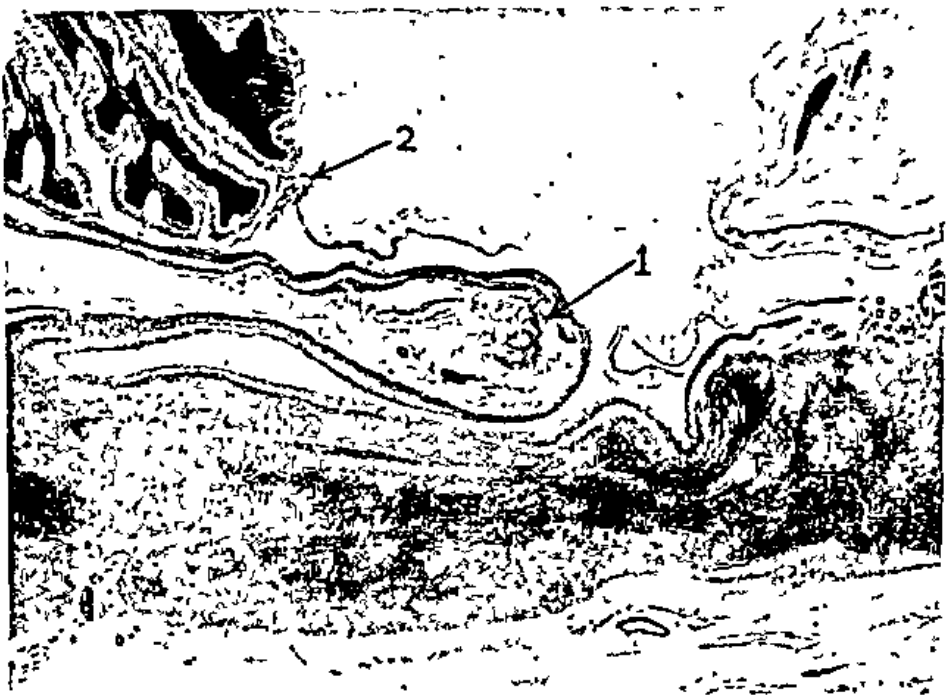


FIG. 9: *Case 15* Mid-sagittal section through hind end of fourth ventricle. The septum, buckled towards the right, bears an abortive cerebellar folium (1) near its centre ; a tuft of choroid plexus lies above it (2). H and E. × 4

The histological nature of the membrane closing the hind end of the fourth ventricle leaves no room for doubt that it is a developmental abnormality: a conclusion that agrees well with the clinical picture. The appearances are closely similar to those described by Taggart and Walker. It may be, as they suggest, that the cause of the malformation is delay in opening, or absence, of the foramen of Magendie. In their view such a course of events is not necessarily followed by severe and progressive internal hydrocephalus since

dialysis of the cerebro-spinal fluid may take place through the membrane. But the burden of proof concerning this point rests with them. They also raise a diagnostic point in radiography: in their cases it was observed that the impression of the lateral sinuses rested on the postero-inferior portion of the parietal bones instead of on the occipital bones; this they regard as due to retardation of the normal migration of the confluent and transverse sinuses posteriorly during the latter part of foetal life. Review of the radiograms of the present case did not confirm the presence of this feature, but, since the films were unsuitable for this particular examination, no categorical statement can be made.

Spina Bifida

It is generally recognized that spina bifida, especially the advanced form known as meningo-myelocele, is frequently associated with internal hydrocephalus. The nature of the association has excited curiosity for many centuries and was commented upon by Morgagni (1761) in his "De Sedibus et Causis Morborum", where he complains rather bitterly of certain of his contemporaries who thought that these watery tumours of the spine derived their contents from the urinary bladder! Morgagni took the view that the hydrocephalus was the primary disorder and that the excess of fluid caused the bulging of the sac. He observed that a discharge of fluid from the spinal defect is accompanied by a decrease in the hydrocephalus. Also the sealing up of a fistulous spina bifida may be followed by a rapidly increasing hydrocephalus. Why this should be has remained a controversial question.

For descriptive purposes the varieties of spina bifida to be discussed are conveniently divided into:

(1) Meningo-myelocele: cases in which the nervous tissues of the spinal cord are actually spread out and incorporated in the wall of the sac.
(2) Meningocele: cases in which meninges and nerve-roots are the only elements of the spinal cord present in the wall of the sac.
(3) Spina bifida occulta: the least severe form, in which a defect in the laminae is unaccompanied by any similar protrusion of soft tissues. On the contrary the overlying skin may bear a tuft of hair, or a rudimentary tail, or may be dimpled. The subcutaneous tissues may be occupied by a lipoma over the site of a defect.

MENINGO-MYELOCELE: THE ARNOLD-CHIARI MALFORMATION

In 1935, certain observations were reported (Russell and Donald) on a peculiar deformity of the cerebellum and medulla oblongata in ten consecutive cases of spina bifida of this type. This deformity is now generally known as the "Arnold-Chiari malformation", the name given by Schwalbe and Gredig (1907) in their careful description of the anatomy in a series of four cases of this kind. The essential features were outlined by Arnold (1894) and Chiari (1895). They consist of a caudal tongue-like prolongation of the cerebellum (the Arnold malformation) which overlaps, and is firmly bound down to, the greatly elongated medulla oblongata (the Chiari malformation). When the two components are dissected apart they are found to enclose the correspondingly elongated fourth ventricle. A large tuft of choroid plexus often occupies its most caudal point. The size of this malformation and the degree to which it occludes the foramen magnum vary from case to case. Characteristic examples are shown in Figs. 10 and 11. Also the precise relationships of the malformation to the spinal cord vary. In some instances there is kinking of the deformed

medulla upon the cord, as shown in Fig. 10. Thus a transverse section of the system near the lower extremity of the malformation will bear an outline resembling the figure 8, as pointed out by Schwalbe and Gredig. In other instances the malformed medulla continues into the spinal cord without a kink. But whatever the arrangement, the spinal cord gives the impression of being displaced caudally into the spinal canal. Thus the segmental roots throughout the cervical region run upwards towards the foramen magnum to gain their dural exits. Towards the thoracic region they straighten into a horizontal direction and thereafter pursue the usual caudal course. The cranial nerve roots are greatly elongated, especially those that arise from the medulla oblongata.

The close association of hydrocephalus with this severe form of spina bifida has been noted in many communications upon the subject. Likewise the constancy with which the Arnold-Chiari malformation is to be found in this condition has been generally recognized since our publication in 1935. Since that year many further opportunities for personal investigation of these cases have arisen and no example of meningo-myelocele has been examined without finding an associated Arnold-Chiari malformation. Nor has reason so far been found for abandoning the theory, put forward in 1935, in explanation of the complicating hydrocephalus. According to this a communicating hydrocephalus may arise from displacement of the fourth ventricle foramina into the spinal canal, when accompanied by obstruction to the reflux of cerebro-spinal fluid into the cranial cavity due to plugging of the foramen magnum by the

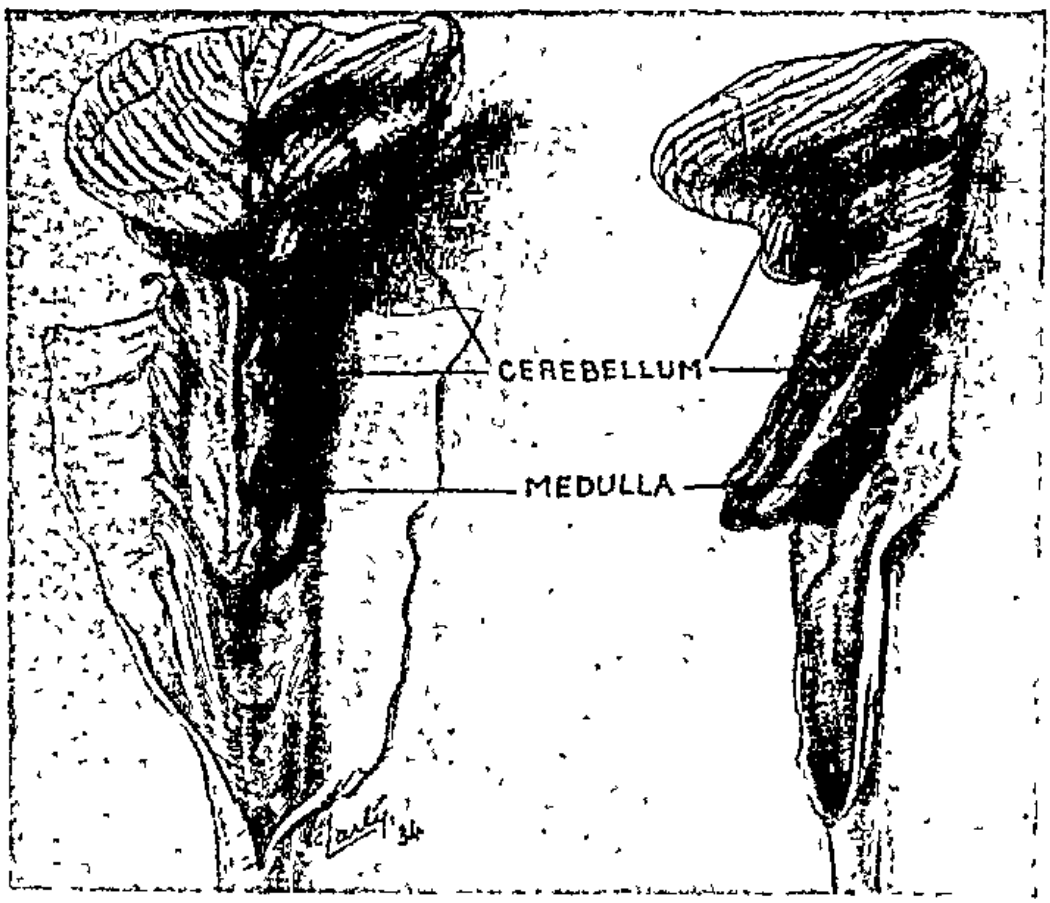


FIG. 10: Posterior and lateral views of the Arnold-Chiari malformation in a case of meningo-myelocele. (By kind permission of the Editor of *Brain*)

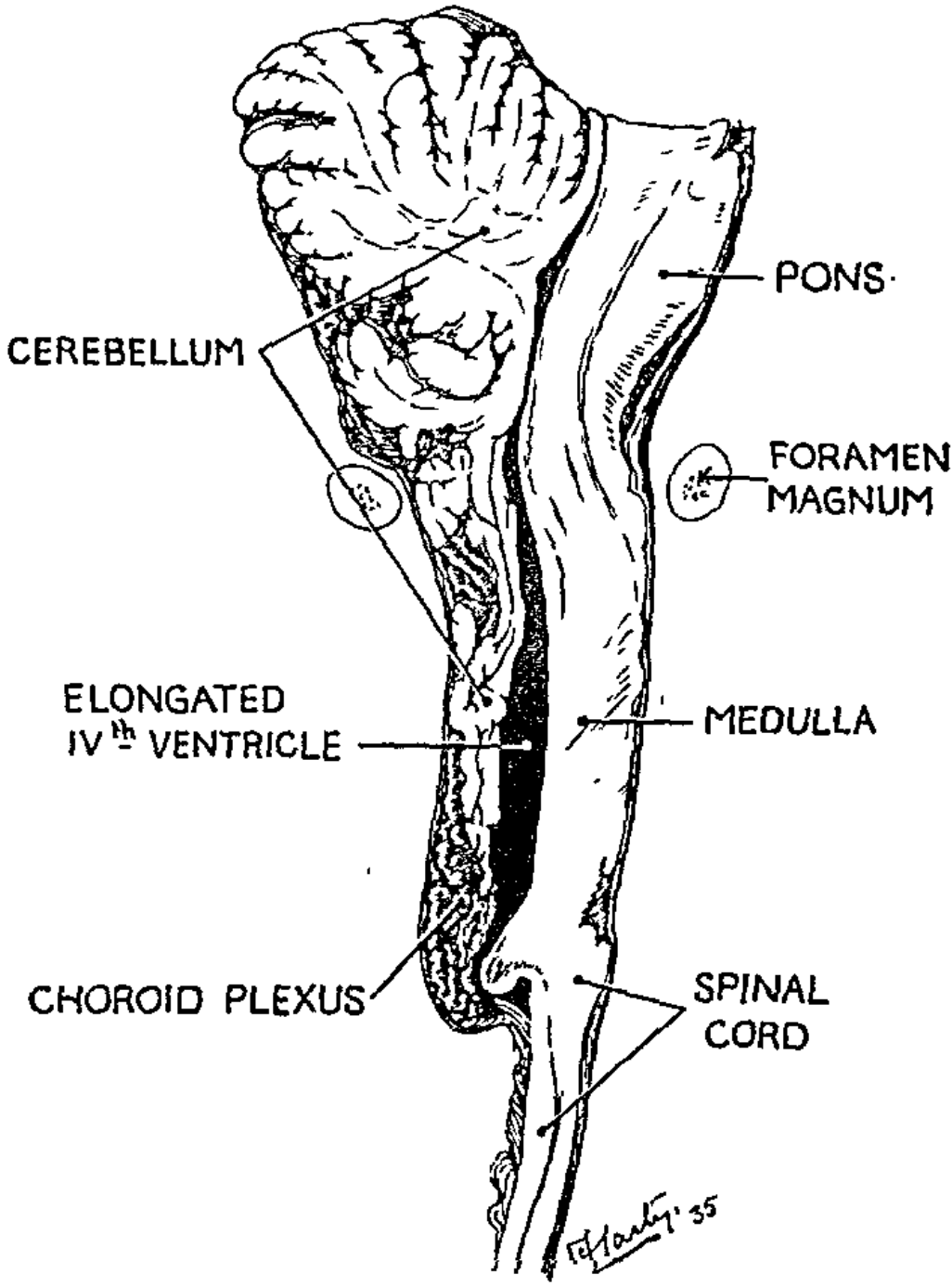


FIG. 11: Median sagittal section of the brain-stem in another case of meningo-myelocele showing relationships of structures to foramen magnum. (By kind permission of the *Editor of Brain*)

Arnold-Chiara malformation. It will be recalled that the amount of fluid that is capable of being absorbed from the spinal theca forms but a small proportion of the whole (Dandy, 1921 a). There are several points in support of this thesis. First, if particulate matter, such as India ink, is injected into the ventricular system before death it will be found, at autopsy, that the greater part of the pigment is collected in the subarachnoid space of the spinal cord, whereas traces only are as a rule to be found at the base of the brain. Likewise, should an ascending purulent infection take place within the spinal canal, there is minimal involvement of the leptomeninges at the base of the brain—sometimes

too little to be visible to the naked eye—while spread into the ventricular system with conspicuous pyocephalus is the rule. There is also the common observation that excision of the sac in spina bifida is sometimes followed by hydrocephalus where none existed before, or the existing hydrocephalus is exaggerated. This led to the demonstration by Penfield and Cone (1932) of the absorbing capacity of the walls of the sac, and their well-reasoned view that this structure acts as a mechanism for the passage of cerebro-spinal fluid into the blood stream. The initiation of hydrocephalus by removal of the sac is readily understood if it is conceded that the Arnold-Chiari malformation in such cases creates a degree of blockage at the foramen magnum sufficient to prevent an adequate return of cerebro-spinal fluid to the cranial cavity. The compensating mechanism provided by the sac may suffice to prevent hydrocephalus in some instances, and to keep it within bounds in others. Support for this explanation will be found in the description of cases of meningocele. It may be noted, however, that the precipitation of hydrocephalus by operative removal of the sac in meningocele is dismissed as a myth by Ingraham and Hamlin (1943).

It has been stated above that hydrocephalus commonly accompanies meningomyelocele with its attendant Arnold-Chiari malformation. Yet on occasion a newborn child may display the latter deformities without enlargement of the head. In the series of cases published in 1935 (Russell and Donald) there were two such examples, and in these it was pointed out that the existence of a fistula at the site of the spinal defect allowed the escape of cerebro-spinal fluid. In one of them it was shown that dye, injected into the lateral ventricle before the necropsy was started, escaped freely with the fluid from the fistula ; in the other, which survived for eleven days, an ascending infection took place leading to pyocephalus. From such observations it is clear that the Arnold-Chiari malformation does not impede free communication between the ventricles and the spinal canal. An alternative view of the mechanical nature of the obstruction at the foramen magnum has been offered by van Houweninge Graftdijk (1932). He suggests that the Arnold-Chiari malformation acts as a valve which permits the passage of fluid from the spinal canal into the ventricles, but obstructs circulation in the opposite normal direction. It is difficult, however, to reconcile this theory with the observations recorded by others as well as ourselves.

Lichtenstein (1942) attributes the development of hydrocephalus in cases of spina bifida to stenosis of the aqueduct, caused by traction upon and elongation of the mid-brain. He and others (Ogryzlo, 1942 ; Alexander, 1942) relate this traction to the tethering of the spinal cord at the site of the vertebral defect. They attribute the Arnold-Chiari deformity to the same mechanical force. There are obvious objections to this interpretation: first, the absence of the Arnold-Chiari deformity from all cases of spina bifida occulta so far examined by the writer and from certain cases of lumbo-sacral meningocele where the spinal cord is tethered in the sacral canal (see below, p. 32) ; secondly, the presence of the deformity in association with a high level of the spina bifida as in Case 16, with a high thoracic meningocele (p. 26), and again in the remarkable case reported by Penfield and Coburn (1938) where the spinal defect involved the third thoracic segment. Thirdly, examples of the Arnold-Chiari deformity have been reported without the association of spina bifida (McConnell and Parker, 1938 ; Aring, 1938) ; in these, however, the possibility of spina bifida occulta was not entirely ruled out. Lichtenstein's theory that a state of

tension exists along the neuraxis in these cases of spina bifida is based upon his postmortem dissection of his Case 1 (*loc. cit.*). In this he exposed the spinal cord and the Arnold-Chiari malformation with the brain in situ, then opened the dura and divided the cord through the mid-cervical region. He then observed that "the entire brain stem suddenly moved upward, as though it had previously been tied down". He does not mention the position of the head during this operation. This, however, is most important: if the neck is flexed a state of tension is normally set up throughout the length of the spinal cord, and division at any level of the exposed cord will be followed by a variable separation of the divided surfaces (O'Connell, 1946). Repetition of Lichtenstein's manœuvre in an infant with a meningo-myelocele of the lumbo-sacral region, and a well-developed Arnold-Chiari malformation which extended for a distance of 3·5 cm. below the arch of the atlas, revealed no such springing apart of the divided segments when the neck was extended; but when the neck was flexed a gap of several millimetres was immediately created. This attractive theory of caudal traction cannot therefore be maintained. However, the curious cephalad course taken by the upper spinal roots in order to gain their dural exits can only mean that the segments concerned lie at an abnormally low level in the vertebral canal. In certain instances it has appeared as though the upper cervical segments were telescoped: there is little doubt that the cord as a whole is often abnormally short. But there is no evidence, from actual comparison of transverse measurements with normal controls, that there is any hypoplasia of the cord. There is thus at present no alternative theory to offer in explanation of the Arnold-Chiari malformation: it appears probable that it takes place at an early stage of embryonic development, perhaps at the stage of closure of the medullary canal, as suggested by Schwalbe and Gredig.

It has been stated above that a certain variability in the anatomical details is demonstrable in any series of cases of meningo-myelocele. It might be expected therefore that even greater variations would be found on extending the search amongst the lesser degrees of spina bifida—namely, meningocele and spina bifida occulta. The pathological anatomy of the brain stem has been described in relatively few of these in the literature. They are, however, instructive in relation to the present enquiry, and hence it is proposed to give details of six cases of meningocele, and of two cases of spina bifida occulta, that have been personally investigated.

In the six cases of meningocele, two showed the development of an Arnold-Chiari malformation, one a Chiari malformation alone, while the remaining three were devoid of this abnormality. Neither of the two cases of spina bifida occulta displayed the malformation.

MENINGOCELE

Cases with Arnold-Chiari Malformation

Case 16: The clinical notes of this case were kindly supplied by Dr. Helen Mackay, under whose care the infant had been admitted to hospital.

J.F., a female infant aged 5 months, and the first child of her parents, was born with spina bifida of the upper thoracic region, in spite of which she progressed favourably up to the age of 7 weeks when she became drowsy and took her feeds badly. When admitted to the Queen Elizabeth Hospital, Hackney Road, on the following day she appeared well nourished (weight 9 lb) but lethargic. The head showed slight oxycephaly, the fontanelles were slightly bulging and the sagittal suture was widely patent. A meningocele was present over the upper thoracic region. Both upper limbs were flaccid and no movement was elicited in them except in the hands. Grasp was fairly good on both sides. The lower limbs appeared normal. Subsequently the power of movement improved considerably in the left upper limb, but only slightly in the right. She was discharged home after 9 days and was not seen again until the

age of 5 months, when she was brought back with the story that, in the previous night, she had "become limp all over" and had had a convulsion lasting for a few minutes, following which she had remained lethargic and developed increasing difficulty in breathing

On examination: There was marked stridor with recession of the chest wall. The child appeared semi-conscious, and all limbs were flaccid and apparently paralysed. Coarse adventitious sounds were heard in all areas over the lungs. Death took place within 24 hours of admission.

Necropsy: (P.M. 43/1946) was performed by the writer. *Broncho-pneumonia: Internal hydrocephalus: Arnold-Chiari malformation: Spina bifida.* Apart from broncho-pneumonia significant changes were confined to the central nervous system.

Examination of head: There was slight oxycephaly, with moderate expansion of the head, which measured 42 cm. in circumference. The anterior fontanelle measured 4·5 × 3 cm., but there was no gaping of the sutures. The bones of the vault, especially the parietal bones, showed marked craniotabes. The cerebral convexities were flattened, and the cerebral substance was reduced in thickness from 2·5 cm. in the frontal parasagittal region to 1 cm. at the occipital poles and to translucency over the temporal poles. The ventricles were symmetrically distended by clear colourless cerebro-spinal fluid. Both the ependyma and the leptomeninges appeared normal. The aqueduct was of normal size (0·1 cm. in diameter) The foramen magnum was filled by a well developed Arnold-Chiari malformation, 3·5 cm. long (Fig. 12), containing a tuft of choroid plexus at its caudal end. It extended down the vertebral canal to within 2·5 cm. of the spinal defect.

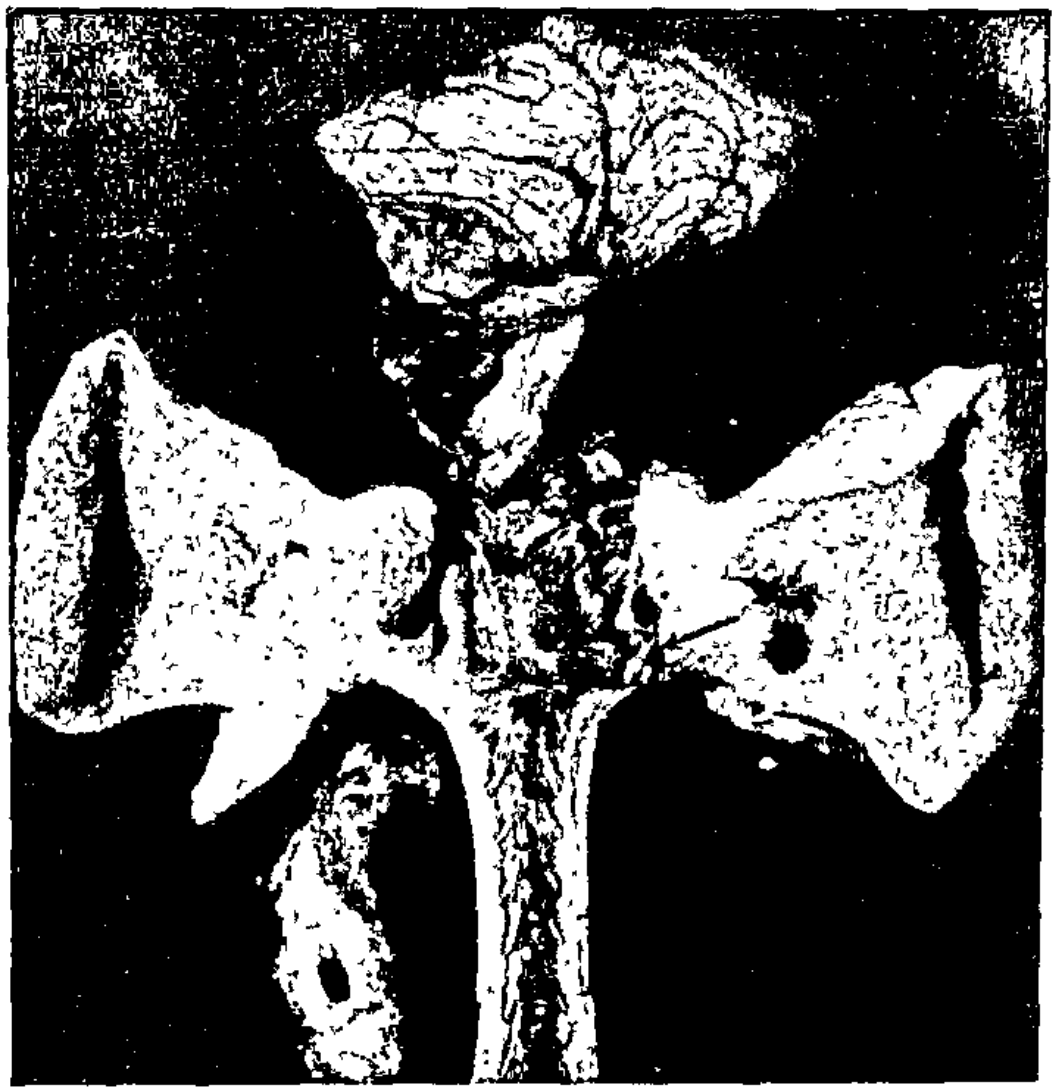


FIG. 12: *Case 16:* The globular mass at the site of the spina bifida has been divided midsagittally. The club-shaped process of neural tissue (arrow) protruded through the laminar defect (shown as separate specimen on left). The cerebellar component of the Arnold-Chiari malformation has been pinned back to expose the elongated fourth ventricle

Spinal cord. A globular fluctuant mass, measuring 7 5 cm. in diameter, covered for the most part by smooth wrinkled skin but capped by translucent pearly-grey epidermis, overlay an oval defect (0 8 by 0·6 cm.) in the laminae of the first and second thoracic vertebrae. On median sagittal section the mass was composed of homogeneous myxomatous tissue except at its base where a sac, 2 5 cm. in diameter, lined by a continuation of the dura, enclosed a club-shaped process of neural tissue arising from the posterior aspect of the spinal cord. The narrow pedicle of the process, with its sheath of dura, passed through the laminar defect (Fig. 12). Within the sac the process was linked to the dura by a delicate cobweb of silky strands. The texture of the process was soft and gelatinous, its apex being cystic.

The lower cervical and upper thoracic segments at the site of the defect appeared to be telescoped, as shown by the radiation of the roots towards the area. All the cervical roots took a cephalad direction from the cord to the dura, and those of the lower cervical segments were considerably elongated and flattened. From the upper thoracic region caudally the spinal cord appeared normal On section there was syringomyelia of the cervical cord in the segment immediately above the site of the defect. The remainder of the cervical cord showed yellowish discoloration and obscuration of the normal pattern.

Microscopic examination: The club-shaped process is composed of neuroglial tissue devoid of neurones. It contains a branched diverticulum of the central canal of the spinal cord derived from the syringomyelic cavity immediately cephalad. The latter provides an offshoot in the posterior median raphe which skirts the posterior surface of the cord to enter the pedicle of the process. The central canal caudal to the spina bifida resumes its normal anatomy. The anterior horn cells are not obviously changed, but there are a few minute haemorrhages in the central grey matter.

The paresis of the arms in this case was presumably due in part to the syringomyelia of the cervical enlargement, and in part to traction upon the nerve-roots, which appeared elongated and flattened on dissection. The fluctuating character of the paresis may well have been due to variations in the intrathecal tension at different times. A surprising degree of internal hydrocephalus was present in spite of the rather slight enlargement of the head. This disparity has been noted by others in cases of spina bifida (Shapiro and Tosti, 1940). An appreciable degree of oxycephaly was, however, also present, so that the volume of the cranial cavity was greater than the measurement of the circumference would indicate.

The case illustrates the association of high spina bifida with a well-marked Arnold-Chiari malformation. Though some degree of traction may well have been exerted from below upwards at the site of the meningocele, it is difficult to attribute the Arnold-Chiari malformation to this mechanism. Nor can the internal hydrocephalus be explained as the result of traction upon the mid-brain, as postulated by Lichtenstein (1942), since no stenosis of the aqueduct was demonstrated.

Case 17: C.H., a female infant aged 7 months (R.I. 32525/1944). Birth was premature at 7 months, the weight being 4 lb. In the upper lumbar region there was a swelling which, at the time of birth, was about 3 cm. in diameter, but grew to 4 cm. by the time she was examined at hospital. At the age of 6 months fluid began to ooze from its surface. The infant appeared normal in other respects, and was able to move all limbs.

On examination: The head measured 44 5 cm. in circumference and was asymmetrical, the right frontal region being more prominent than the left. There was a slight cracked-pot note on percussion. The anterior fontanelle was wide, tense and bulging. The rest of the neurological examination revealed no abnormality apart from the meningocele, which was superficially ulcerated.

Operation: Excision of the sac. This proved to be multilocular and was united with the contents of the spinal canal by a stalk, about 2 cm. long and about 0·6 by 0·8 cm. thick, of fibro-lipomatous tissue. Cerebro-spinal fluid escaped from the opening before it was closed. On histological examination the sac showed ulceration of the epidermis over its centre, and considerable purulent infiltration of the subjacent tissues. The walls of the central loculi were composed of collagen and, in places, loose web-like areas of meningeal tissue. No neuroglia or other nervous elements were identified.

The infant appeared to recover well from the operation, but died on the following day with elevated pulse and respiration rate.

Necropsy (R.I. P.M. 428/1944): *Internal hydrocephalus: Arnold-Chiari malformation.* No significant changes were found in other organs. The laminae of the third, fourth and fifth lumbar vertebrae were ununited and the stalk of the meningocele occupied a gap at the level

of the third. At this point a bony spur projected backwards in the mid-line from the body of the vertebrae, traversing the vertebral canal to become embedded in the fibro-adipose tissue occupying the laminar defect. The spinal cord divided into two parts on either side of the spur, becoming united caudally to form a normal conus at the level of the disc between the fifth lumbar and first sacral vertebrae. On section there was syringomyelia of the cord from the eleventh thoracic segment to the point where the cord divided.

The anterior fontanelle was expanded, measuring 7 by 4·5 cm. The interior of the skull showed evidence of pressure, in the deep cupping of the cribriform fossae and diaphragma sellae, hollowing of the clivus and widening of the nerve-root foramina. The cerebral hemispheres were expanded and flattened and, on section, showed considerable internal hydrocephalus, the left ventricle being somewhat greater than the right (Fig. 16). The ependyma appeared unaltered. The aqueduct was greatly dilated, measuring 0·5 by 0·4 cm. The cerebellum was of normal size but the inferior vermis was lacking. As shown in Figs. 13 and 14, an unusual variety of the Arnold-Chiari malformation was present consisting of an elongated and enlarged right tonsil (1·8 cm. long) which was displaced medially to overlap the greatly elongated medulla and fourth ventricle. The left tonsil was small and was displaced laterally. The cervical spinal roots showed the characteristic cephalad course to their dural exits (Figs. 14 and 15); the second thoracic roots were horizontal and thereafter a caudal direction was pursued.

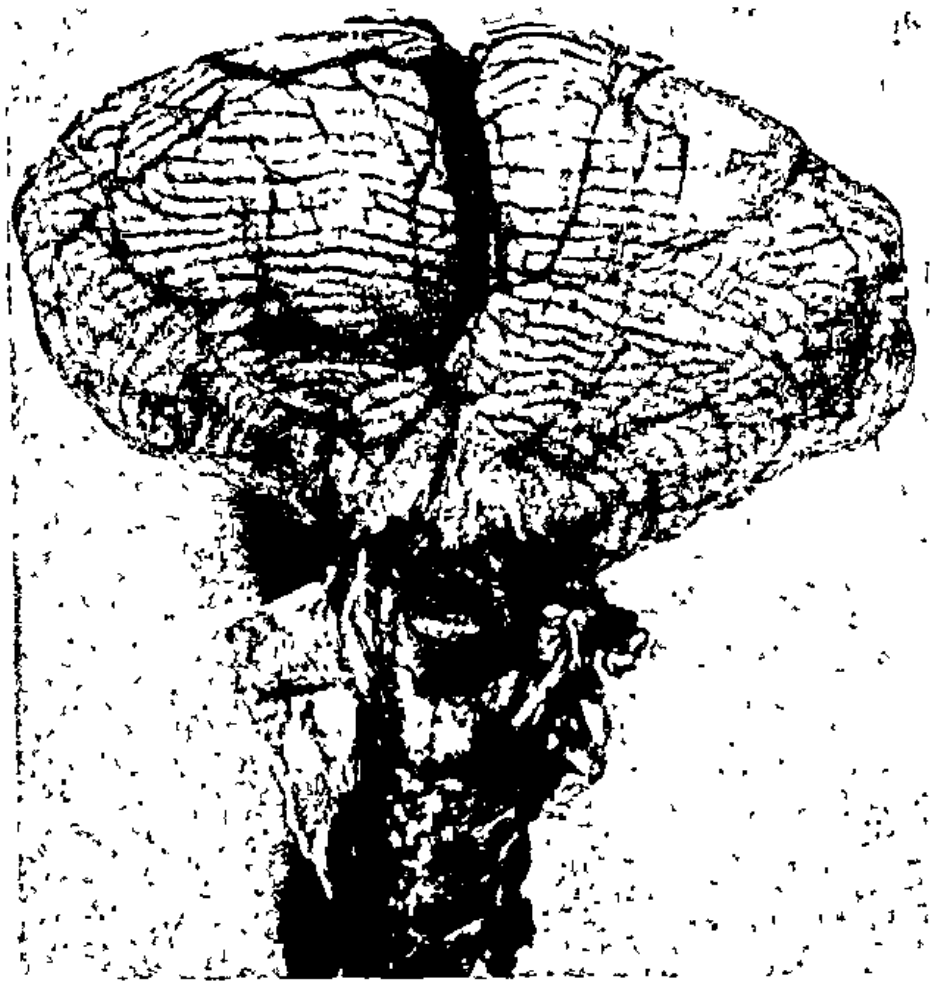


FIG. 13: *Case 17:* Dorsal view of malformation. The enlarged right tonsil has been freed by dissection from the medulla

FIG. 14: *Case 17:* View from left to show obliquity of roots

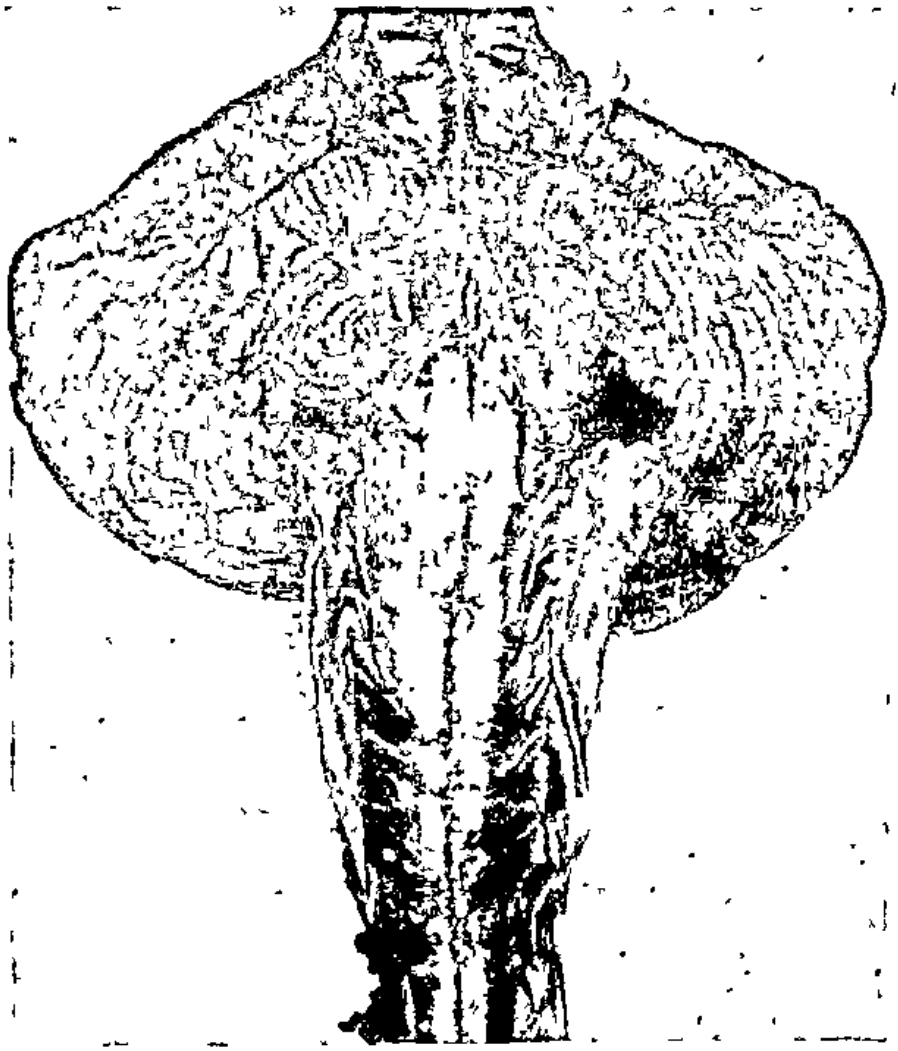


FIG. 15: *Case 17:* Ventral aspect showing elongation of medulla and obliquity of roots

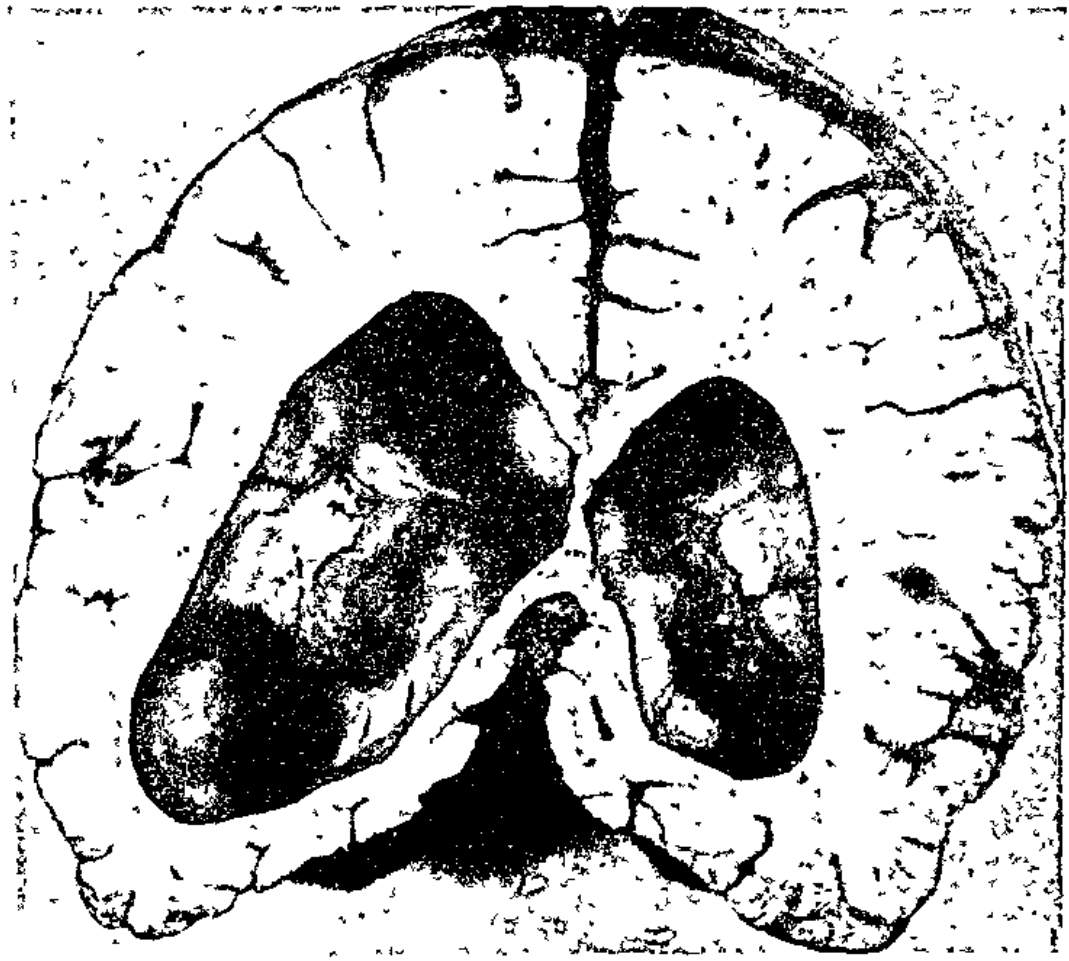


FIG 16: *Case 17:* To show dilatation of lateral ventricles

Case with Chiari Malformation alone

Case 18: Female infant, aged 15 weeks (Reg. No. 21882/1934). Full details have already been published (Russell and Donald, 1935) In summary, the infant was admitted to hospital when three days old for the repair of a cystic lumbo-sacral meningocele. There was no evidence of hydrocephalus. The operation was followed by purulent meningitis and pyocephalus, and the child died 11 weeks later.

Pathological examination established the following relevant points. The spinal defect involved the laminae of the lowest three lumbar and all sacral vertebrae. The spinal cord extended to the tip of the sacrum (Fig. 17), where it ended in a bulbous expansion. There was no evidence of obstruction at the foramen magnum although a certain degree of malformation was present. This involved the medulla oblongata alone (Fig 17). It was slightly elongated into the cervical canal with a concomitant upward deviation of the first and second cervical roots. Below this the roots took a horizontal and subsequently a caudal direction. The cerebellum appeared normal.

This case is quoted anew because it is different from the two described above, and so far is the only example personally examined in which this limited form of Arnold-Chiari malformation has been seen. According to our theory it would not be expected to produce internal hydrocephalus because it is not of an obstructive character. Again we have a clear demonstration of the fact that retention of the tip of the spinal cord at the caudal end of the vertebral canal does not, in itself, cause elongation of the brain-system or hydrocephalus from stenosis of the aqueduct, as postulated by Lichtenstein.

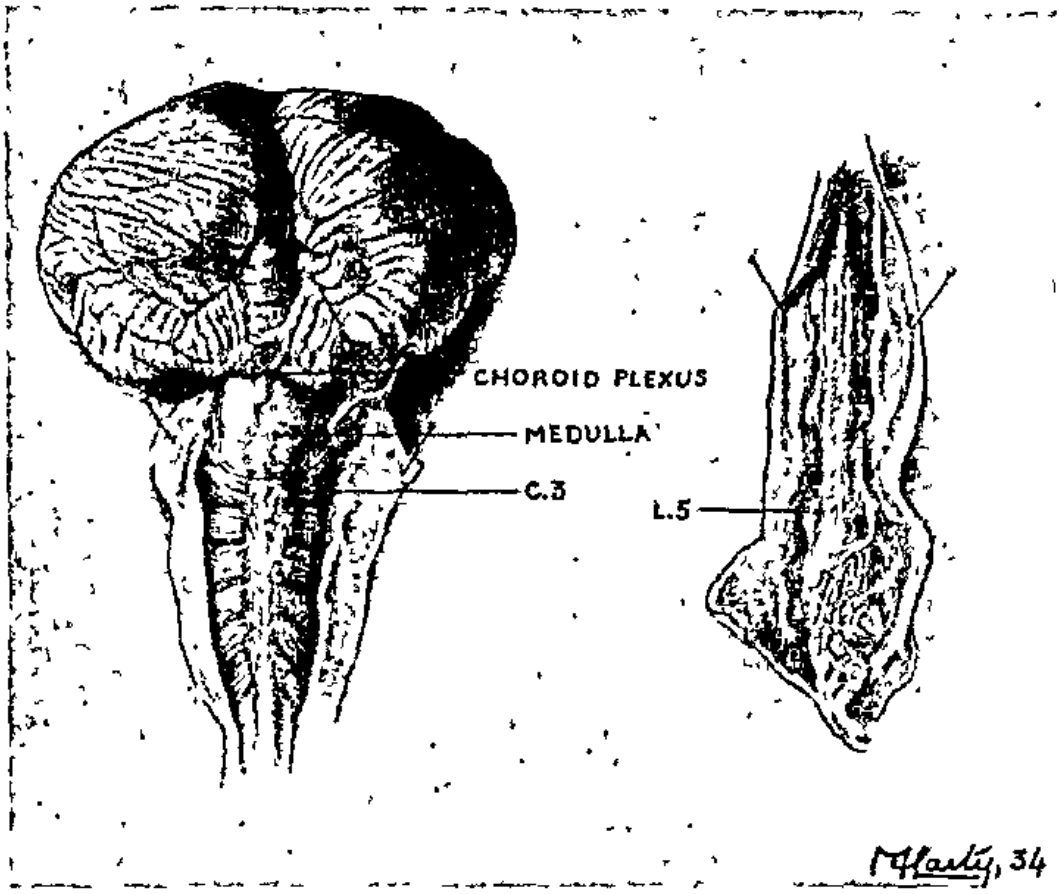


FIG. 17: *Case 18:* Dorsal view of hind-brain to show Chiari malformation and deformity of lumbo-sacral cord (By kind permission of the Editor of *Brain*)

Cases without Arnold-Chiari Malformation

Case 19: A.C., a male infant aged 11 weeks (R.I 12380/1943). At birth, which was normal, a lumbo-sacral meningocele was observed which discharged on the following day. Subsequently it became dry. The head was not enlarged. When admitted, at the age of 6 weeks, there was retraction of the head, but no stiffness of the neck. The head was slightly enlarged (38 cm in circumference) but the fontanelle, though full, was not bulging. The sclerotics were visible above the irides in a manner suggestive of hydrocephalus A firm, globular, epithelialized swelling, about 15 cm. in circumference, was attached by a narrow pedicle over the lumbo-sacral spine. Its surface was dry. There were no abnormal neurological signs. Three days later an *operation* was performed for the removal of the meningocele. A minute canal, measuring 2 to 3 mm. in diameter, was found on its deep aspect passing through the muscles to the spine, but there was no appreciable leakage of cerebro-spinal fluid.

Histological examination of the operation specimen confirmed the diagnosis of meningocele. A microscopic abscess, containing Gram-positive cocci, was found near the centre of its deep aspect.

On the day following operation the temperature rose to 100° F. and appropriate doses of sulphathiazole were given four-hourly to check the possible spread of infection from the site of operation. Nevertheless signs of meningitis developed, accompanied by progressive expansion of the skull which, when the child died 5 weeks after operation, had attained a circumference of 42 cm.

Necropsy (R.I. P.M. 353/1943): No significant changes were observed apart from those in the central nervous system. The laminae of the sacral and fifth lumbar vertebrae were ununited and beneath this defect the lumbo-sacral segments were tethered so that the cauda equina and lumbar enlargement were not developed. Evidence of meningitis was limited to a slight opacity of the membranes in the lower thoracic and lumbar segments. There was gross internal hydrocephalus, involving all ventricles; the aqueduct measured 0 5 cm. in diameter. At the foramen magnum the medulla was closely enveloped by a cone-shaped mass of cerebellar tissue (Fig. 18) which proved, on dissection, to be composed of the tonsils. When separated, a translucent membrane was found at the site of the foramen of Magendie (Fig 19). The roots of the second cervical segment lay horizontally within the theca; below this level

they were directed caudally. There was great ballooning of the tissues at the foramina of Luschka, forming a translucent bleb, about 1 cm. in diameter, on either side. There was no demonstrable elongation of the brain-stem. Chronic inflammatory changes were observed in the choroid plexuses of the lateral ventricles. Finely granular ependymitis was also present. *Microscopic examination:* In a mid-sagittal section the membrane occluding the foramen of Magendie is composed, above and below, of fibrillary neuroglia lined, towards the ventricle, with a layer of ependymal cells. The central third of the structure is occupied by a flattened mass of choroid plexus. Externally the membrane is coated with the pia, which is reflected on to its surface from the adjacent cerebellum and medulla oblongata. The white matter of the adjacent cerebellar tonsil has undergone gliosis with partial loss of its myelin. Sections from other parts of the brain reveal slight chronic leptomeningitis and subacute purulent ependymitis. There is perivascular cuffing of the subependymal blood-vessels with lymphocytes. The choroid plexuses are embedded in granulation tissue containing a considerable number of collagenous fibres and chronic inflammatory cellular infiltration. A transverse section through the lumbar cord shows slight meningitis, mostly confined to the *ventral fissure ; the grey matter is infiltrated with lymphocytes and neutrophil leucocytes.*

FIG. 18: *Case 19:* To show considerable matting of meninges about the tonsils

In the absence of an ascending meningitis there can be little doubt that the surgical treatment of this case would have been successful. In spite of the membrane occluding the foramen of Magendie, which was shown microscopically to be a developmental abnormality, there was little evidence of hydrocephalus when the child was admitted to hospital. This state of balance had evidently been maintained by the foramina of Luschka. Their patency was proved by the extension of the infection into the ventricular system, where a low-grade purulent inflammatory reaction was set up. This inflammation however, in its turn, sealed the foramina of Luschka and internal hydrocephalus ensued. The progressive increase of intracranial pressure was responsible for the marked herniation of the cerebellar tonsils which then became impacted in the foramen magnum. At first inspection the cone of cerebellar tissue so

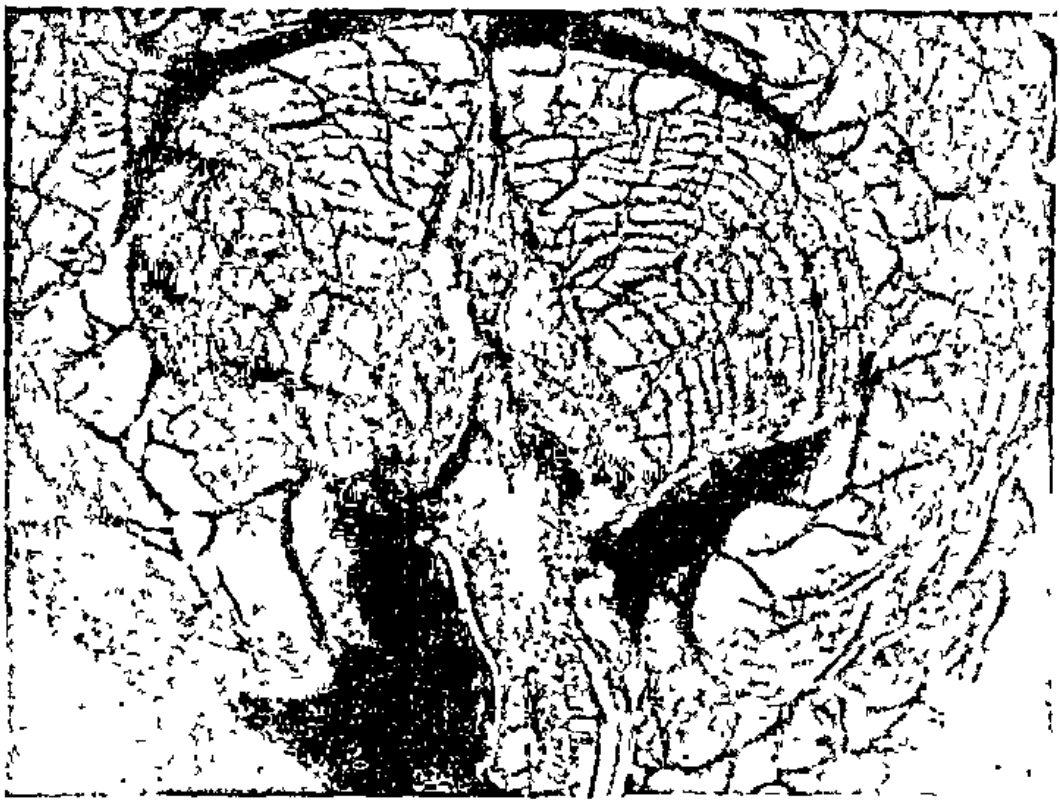


FIG. 19: *Case 19.* On freeing the tonsils the foramen of Magendie is seen to be occluded by a membrane

formed was suspected of being some variant of the Arnold-Chiari malformation, but this was not substantiated by dissection. It may be noted in passing that, though the spinal cord was tethered in the sacral region, there was no evidence of traction upon the cervical nerve-roots nor upon the brain-stem, and there was no stenosis of the aqueduct.

Case 20: M W., female aged 27 (R.I 18055/1943). Incontinence of urine and faeces had been present since birth, and she had had headaches in infancy. In 1938 a colostomy was performed on account of malformations of the pelvic viscera, followed, in 1939, by transplantation of the right ureter into the skin of the abdominal wall, and hysterectomy. In 1939 the left ureter was similarly transplanted. She continued at munition work until six days before death when she returned to hospital on account of inability to replace the left ureteric catheter. Readjustment of the catheter proved ineffective. Radiography showed hydronephrosis of the right kidney and she died in uræmia.

Necropsy. (R.J P M 467/1943): *Fibrino-purulent peritonitis. Left perinephric abscess. Bilateral pyonephrosis. Right renal calculus. Sacral meningocele. Bilateral pes cavus. Persistence of urogenital sinus with failure of development of vaginal canal, failure of downgrowth of uro-rectal septum, and persistence of part of cloacal membrane.*

Examination of central nervous system. All the sacral laminae were ununited permitting the protrusion of a saccular meningocele measuring 6 by 4·5 cm. This was covered by smooth grey wrinkled epithelium beneath which was a layer of adipose tissue. The sac itself was lined with tough glistening grey tissue continuous with the spinal theca. The spinal cord was elongated into the cavity of the sac, gradually tapering into the filum terminale which joined the dorsal wall of the sac a little caudal to its centre. The lumbar enlargement was lacking, the lumbar roots passing horizontally to their exits. The second, third and fourth pairs of sacral roots traversed the sac and it was remarkable that the third and fourth pairs, after entering the sac, ramified in the more caudal part of its walls and gained no continuity with the spinal cord. The cervical and thoracic segments of the cord appeared normal.

The brain showed slight fullness of the right tonsil, but no evidence of malformation in this region. There was slight dilatation of the lateral ventricles, especially in the body and vestibule. The aqueduct was narrowed, measuring about 0·075 by 0·05 cm., between the anterior and posterior corpora quadrigemina; throughout the remainder of its course it appeared normal.

Microscopic examination At the point of narrowing the aqueduct is subdivided into two parts: the more dorsal corresponds to the lumen seen with the naked eye, while the ventral is represented by a grouping of ependymal cells about a central core of acellular fibrillary glia. The appearances are thus indicative of a "forking" of the aqueduct with secondary obliteration by glia of the smaller, ventral channel Sections from blocks taken from either side of this level of the mid-brain show no histological abnormality

Sections from the wall of the meningocele at the terminations of three of the sacral nerves show dense collagenous tissue including a plexiform arrangement of bundles of myelinated nerve-fibres ; there is no trace of nervous tissue apart from these.

This case displays a number of remarkable features which merit a more general discussion than is relevant here. The important points to be noted are: first, the absence of the Arnold-Chiari malformation although the spinal cord was tethered at the level of the sacrum. Secondly, although a slight degree of internal hydrocephalus was present, and was associated with what appeared to the naked eye to be a simple stenosis of the aqueduct (as already defined, p. 11), microscopic examination showed that this abnormality was due to forking of the aqueduct. The stenosis therefore could not be interpreted as the effect of traction exerted from the caudal part of the neuraxis, in the manner suggested by Lichtenstein. In general, forking of the aqueduct is incompatible with long survival but, as the present case clearly shows, a sufficient degree of patency may be present in one branch of the channel to maintain a normal circulation of cerebro-spinal fluid.

Case 21· J.H , a male infant aged 4 months. At birth a large mass, about the size of an orange, occupied the lumbo-sacral region (Fig 20) There was no evidence of hydrocephalus. An operation for repair of the sac was carried out, but the infant subsequently died from an intercurrent infection. The brain and spinal cord were received for examination from another hospital through the courtesy of Mr. Charles Donald.

Examination of central nervous system· The brain appeared normal, with no dilatation of the ventricular system and no evidence of any malformation in the hind-brain. The cord was accompanied by an elliptical area of skin bearing a puckered scar, measuring 6 5 by 1 cm , overlying the sacrum and fifth lumbar vertebra. The laminae of the second and third sacral vertebrae were defective, and the spinal cord was prolonged to the site of this defect where it expanded into a bulbous mass, up to 1 1 by 0 6 cm. thick, which was firmly adherent to the surrounding dura. On section the cord tissue in this terminal expansion was subdivided by dense grey fibrous tissue. The roots below the first sacral were not identified. There was no morphological differentiation between the lumbar and thoracic segments, the pairs of roots being given off at regular intervals down to the first sacral. The spinal cord appeared otherwise normal both superficially and on transverse section.

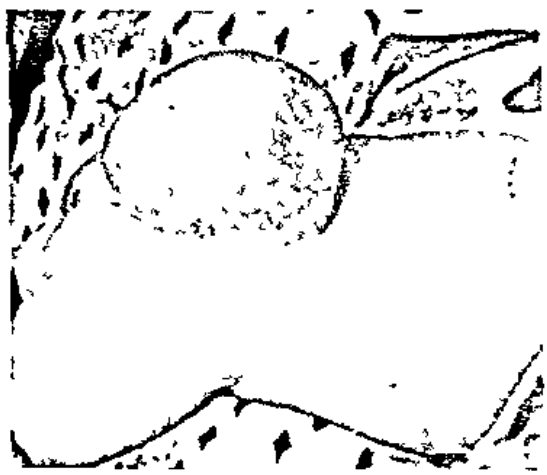


FIG. 20: *Case 21:* Showing lumbo-sacral meningocele

This case provides a good example of sacral meningocele in which no further abnormality of a developmental character was found in the rest of the central nervous system. In spite of the tethering of the cord at this low level in the vertebral canal there was neither an Arnold-Chiari malformation nor stenosis of the aqueduct.

SPINA BIFIDA OCCULTA

Case 22: E.H., female aged 2 months (Reg. Nos. 21687.40815/1936). Birth had been 2 months premature, the weight of the child being about 3½ lb. The head was large then and subsequently became much bigger. The right index finger had been flexed since birth. There had been no convulsions and the infant had increased in weight. When admitted to the London Hospital, at the age of 1 month, the head measured 47·3 cm. and all sutures were widely open. There were no abnormal neurological signs. *Lumbar puncture* yielded clear colourless fluid containing 40 mg. of protein per 100 c.c. and no excess of cells. The Wassermann reaction was negative. When 5 c.c. of indigocarmine were injected into a lateral ventricle the dye was at once reclaimed from the opposite side, but failed to appear in the lumbar fluid at the end of 20 minutes. Later punctures were vitiated by haemorrhage. The dye appeared in the urine at 17 hours. The pressures of fluid in the ventricles and spinal theca were equal at about 170 mm.

Encephalography revealed air in the cisterns below the tentorium and perhaps in the fourth ventricle, but none in the lateral ventricles. Death followed two hours after an operation for posterior ventriculostomy with division of the right wing of the tentorium.

Necropsy (P.M. 221/1936): *Internal hydrocephalus: Forking of aqueduct: Sacral spina bifida occulta: Multiple congenital deformities including absence of left kidney, double ureter and pelvis in large right kidney, malformation of ribs with lower thoracic scoliosis and funnel-shaped deformity of sternum*

Examination of brain: The cerebral substance was greatly thinned, being membranous on the mesial aspects of the occipital lobes, and up to 2 cm. thick over the frontal poles. The septum pellucidum was replaced by an aperture uniting the lateral ventricles and bridged over by the greatly thinned fornix. The ependyma was everywhere smooth and glistening. The choroid plexuses were atrophied. The aqueduct was visible, on transverse section, as a pinpoint meatus less than 0·05 cm. in diameter beneath the anterior corpora quadrigemina; caudal to this it attained this measurement, being first slit-like and then, beneath the posterior corpora quadrigemina, again rounded. There was no trace of the Arnold-Chiari malformation at the foramen magnum. The cerebellum, however, bore in its leptomeninges a minute dermoid cyst, measuring 1·2 × 0·7 cm., and containing a single coarse black hair. This cyst occupied the mid-line and was tucked in between the closely apposed lateral lobes over the upper part of the vermis. Defect (1·8 by 1·1 cm.) in sacral laminae beneath dimple in skin 2·5 cm. above anus. Slight focal dilation of central canal in seventh cervical segment of otherwise normal spinal cord.

Microscopical examination of the aqueduct showed the condition of "forking" already described (p. 14). This appeared to involve the whole length of the aqueduct, the larger, dorsal channel being the lumen which had been visible to the naked eye.

Case 23: M.W., a woman aged 49 years (Reg. No. 21183/1931). She had had frequency of micturition all her life. For 20 years there had been numbness of the right leg. For the past 5 years there had been incontinence of urine, an ulcer on the sole of the right foot, numbness of the left big toe, and also of both arms on awakening at night.

Examination revealed a funnel-shaped depression, about 5 cm. in diameter, in the mid-sacral region. In the centre of this was a pit admitting the tip of a finger, and, on coughing, an impulse was felt at this point. Apart from external squint of the left eye, and nystagmus, the cranial nerves were normal. Movements at the hip, knee and ankle were weak on both sides, especially the right. Tendon jerks were elicited in both legs and an extensor plantar response was present on the left. In the right leg sensation of pin-prick, temperature and vibration was diminished and in the foot all sensation appeared to be lost. In the trunk sensation of pin-prick was normal except in the right lower abdomen and right buttock. The lower abdominal reflexes were absent.

Laminectomy disclosed a massive lipoma in the lumbo-sacral region which extended from without the theca into the substance of the spinal cord, which was found to be persistent at the level of the sacrum. Part of the tumour was removed and arachnoidal adhesions were divided. Death took place 5 days later.

Necropsy (P.M. 170/1931): *Ascending purulent nephritis: Cystitis: Bilateral hydronephrosis.*

The brain appeared congested and there was a cerebellar pressure-cone. On section no abnormality was found and the ventricular system was normal. A post-anal dimple in the skin was connected to the posterior surface of the coccyx by a fibrous cord, 3·5 cm. long and 0·5 cm. in diameter. The spinal cord was greatly elongated, its caudal extremity being retained in the sacral canal. From the eighth thoracic segment the spinal roots showed a decreasing obliquity in their course towards their dural exits until, in the upper two lumbar segments, this became reversed in the cephalic direction. From this level caudally the rest

of the cord was involved in a lipoma which formed a sausage-shaped mass measuring 7·5 cm. in the axis of the cord and about 2·8 cm. in diameter. Its surface blended with the enveloping dura mater. At its caudal extremity the filum terminale was identified. On section the spinal cord above the level of the tumour showed no abnormality beyond pallor of the column of Goll. The cord formed a crescentic slip about the left ventro-lateral border of the tumour, becoming increasingly compressed towards the greatest diameter of the latter and unrecognizable below the second sacral segment. The tumour thus was extra-medullary.

Case 23 recalls the example of spina bifida occulta in an 8-9 months' foetus, described by Bland-Sutton (1888) in which the spinal cord extended to the tip of the coccyx and ended there in a fatty swelling of the size of a large nut. There were several associated congenital maldevelopments involving other tissues.

These two cases of spina bifida occulta have been quoted in some detail because they illustrate certain important points in relation to spina bifida as a whole. First, although the caudal end of the spinal cord was retained at the sacral level in Case 23 there was no malformation of the Arnold-Chiari type at the foramen magnum. Though traction must have existed, its effect seems to have resulted simply in the elongation of the lower thoracic and lumbar segments with obliteration of the normal lumbar enlargement. There is certainly no evidence that this traction affected the brain-stem; there was no abnormality of the aqueduct in this case, and no hydrocephalus. Nevertheless, as shown by the first of the two cases, hydrocephalus may co-exist with spina bifida occulta and may be due to some associated maldevelopment—in this instance forking of the aqueduct.

Deformities of the Base of the Skull

PLATYBASIA

This is a deformity of the skull in which the basal angle formed by the basi-sphenoid and the clivus (normally 130° to 140°) is increased. It is associated with foreshortening of the basioccipital bone and a variety of bony malformations about the foramen magnum whereby the margins of the foramen and adjacent parts of the occipital bone are pressed into the cranial cavity. As a result the odontoid process may be brought into the posterior fossa, thus further narrowing the foramen magnum and pressing upon the ventral surface of the medulla oblongata (basilar impression). It is generally agreed that congenital maldevelopment is the basis of the deformity as a rule, and Klippel-Feil's disease may form a part of the syndrome (List, 1941), though de Vet (1940) considers the evidence for such a connection as unconvincing. Platybasia may also arise as a secondary development in diseases that cause softening of the bone, and hence moulding, as the result of pressure. A well-documented case has been reported by Wycis (1944) in association with osteitis deformans. A variety of neurological disturbances arises from pressure of the bone upon nerve-roots and the brain-stem. Moreover the foreshortening of the basi-occipital results in a dislocation of the brain-stem whereby the medulla oblongata and the cerebellar tonsils are pushed into the upper cervical canal. When this is associated with narrowing of the foramen magnum, internal hydrocephalus is likely to arise (List, 1941). The mechanism of the hydrocephalus is thus closely similar to that postulated in connection with the Arnold-Chiari malformation. In fact the superficial similarity of the anatomical picture has led several observers to use this name for the cerebello-medullary dislocation found in platybasia. But since there is no evidence of any essential malformation of the neuraxis in such cases it would appear preferable to restrict

collateral circulation in cases where the sigmoid sinus has failed to develop.

Dandy (1921 b) demonstrated a conspicuous degree of generalized ventricular dilatation by ventriculography in an achondroplastic subject aged 19 years. The air reached the sulci over the cerebral convexities thus showing that the hydrocephalus was of the communicating type. Moreover, dye injected by the lumbar route was recovered shortly afterwards from a lateral ventricle. Dandy considers that, from the clinical evidence, the hydrocephalus would appear to be present at birth when the head, as in the case described by him, may be so enlarged as to present difficulty in delivery. He suggests that the chondrodystrophy at the base of the skull probably leads to obstruction in the posterior fossa, and hence to the development of internal hydrocephalus. But the yielding of the skull to pressure in infancy leads to a readjustment in the relationship of brain to bone and the condition is not of a progressive character. It is of interest that a similar mechanism is postulated by Grüneberg (1943 b) as the cause of one variety of congenital hydrocephalus in the mouse (see p. 10).

Lissencephaly

This term, according to Walker (1942) was introduced by Owen in 1868 to describe a condition of agyria in which the cerebral hemispheres are smooth and unconvoluted. Few cases have been reported and it appears that hydrocephalus is an inconstant feature. In the case described by Walker, in an infant of 4 months, there was gross internal hydrocephalus. The arachnoid membrane contained relatively little reticulin and was firmly adherent to the cortex and brain-stem. From the associated malformations in this case Walker argues that arrest of normal development took place at about the third month of foetal life with consequent agenesis of the subarachnoid space, which ordinarily opens up at the tenth week. The cerebro-spinal fluid was therefore retained within the ventricular system with resulting hydrocephalus. This mechanism has been postulated from time to time in attempts to explain cases of so-called idiopathic hydrocephalus, but this condition of lissencephaly is perhaps the only class of case in which it can be claimed that such a mechanism has been satisfactorily elucidated.

CHAPTER III

GLIOSIS OF THE AQUEDUCT

THIS subject is conveniently considered in a separate section on account of the obscurity of the ætiology in this condition. Gliosis of the aqueduct must be distinguished from three other conditions which may bear a superficial resemblance to it. First, simple stenosis of the aqueduct which has already been defined and described (p. 11), and which is to be regarded as a developmental abnormality. Secondly, forking of the aqueduct, commonly known as "atresia", which has frequently been confused with occlusive gliosis in the literature. But, as already pointed out (p. 14), the subdivision of the aqueductal channels observed in "forking" follows a consistent pattern, as viewed in transverse sections of the mid-brain, and the two main channels into which the aqueduct divides are separated by normal neural tissue in which gliosis is not demonstrable. Thirdly, a distinction must be drawn between gliosis of the aqueduct and fibrillary astrocytomata of the quadrigeminal plate. It might be considered that the difference between these two conditions would be too obvious to permit of any confusion, and, when the tumour is well developed, the truth of this must be granted. But, owing to their critical situation, tumours arising in the tegmental part of the mid-brain may prove fatal at an early stage of their development, and the distinction then may not be so easy. Such an example is provided by Case 49 (p. 100) which is provisionally classified in the neoplastic group.

Eight examples of gliosis of the aqueduct have been examined in the present series. All were in infants or children, with the exception of one case in an adult. Juvenile and adult types are recognized, and have been described from the clinical standpoint by Pennybacker (1940) from his total of 18 examples of this condition.

In children the onset of hydrocephalus is usually insidious, with gradual enlargement of the skull. Medical advice is generally sought at an advanced stage when visual failure and headache claim attention. Apart from increased pressure the cerebro-spinal fluid is normal, and where the Wassermann reaction has been done it has been negative. Cases in adults are much rarer, but five are reported by Pennybacker in subjects between the ages of 18 and 25. The single example in an adult described here is additional to these.

Macroscopically there is gross dilatation of the third and lateral ventricles, the fourth being normal in size. Externally, it is significant that the quadrigeminal plate is not deformed; in this lies a difference from "forking" of the aqueduct and neoplasms of this region, when deformity is the rule. On longitudinal section the anterior part of the aqueduct is funnel-shaped, the stem of the funnel narrowing to a point, which may be anywhere along its course, where the lumen appears to be entirely occluded. This occlusion may be so limited as to suggest a partition, or it may be prolonged for a distance of several millimetres. Microscopically the essential change is an overgrowth of the subependymal neuroglia, which is of a densely fibrillary character. This may cause displacement, narrowing or even subdivision of the lumen. The following four cases illustrate variations in the histological picture.

Case 24: J.H., female aged 15 months (Reg. No. 23983/1923). The infant appeared normal at birth but, after 3 days, the head seemed unduly large and gradually increased in circumference at the rate of about 2 5 cm. a month until one month before admission, after which no

increase was noted. After the third month of life progressive wasting was observed No relevant family history was elicited.

Examination revealed an enormous degree of cranial enlargement, the circumference being 76 cm. The veins of the scalp were greatly distended. There was marked nystagmus. The infant was greatly wasted but there were no further deformities. Death took place a month after admission, the withdrawal of cerebro-spinal fluid by ventricular puncture having proved ineffective.

Summary of necropsy (P.M. 540/1923): *Lipoid pneumonia. Chronic internal hydrocephalus: Occlusion of aqueduct of Sylvius. Craniotabes.*

Bone of vault nowhere thicker than 0 5 cm. Enormous dilatation of lateral ventricles by somewhat more than 4 litres of clear colourless fluid. Brain substance, 0 4 cm. thick, closely apposed to dura. Cyst, 6 × 5 cm , upon dorsum of cerebellum in subarachnoid space, communicating with left lateral ventricle by an aperture, 4 × 2 cm , in the posterior horn above level of velum interpositum and mesial to calcar avis. No dilatation of fourth ventricle Apparent occlusion of aqueduct of Sylvius by pearly grey tissue. No further malformations, or relevant changes in other organs.

Microscopic examination: Serial sections were prepared from transversely cut blocks through the mid-brain. The appearances are represented by Fig. 23, taken from near the anterior and posterior extremities of the aqueduct respectively. At all levels the normal outline of the aqueduct is indicated by a more or less dense zone of ependymal cells, the nuclei of which produce the pattern shown in the microphotographs On higher magnification many of these cells are seen to form minute tubules, or rosettes In places they expand into larger channels which are mainly concentrated at the ventral end of the area throughout the series. Towards the hind end a persistent channel appears in addition in the central fibrillary glia and this gradually enlarges towards the fourth ventricle. There is no histological evidence of any inflammatory reaction.

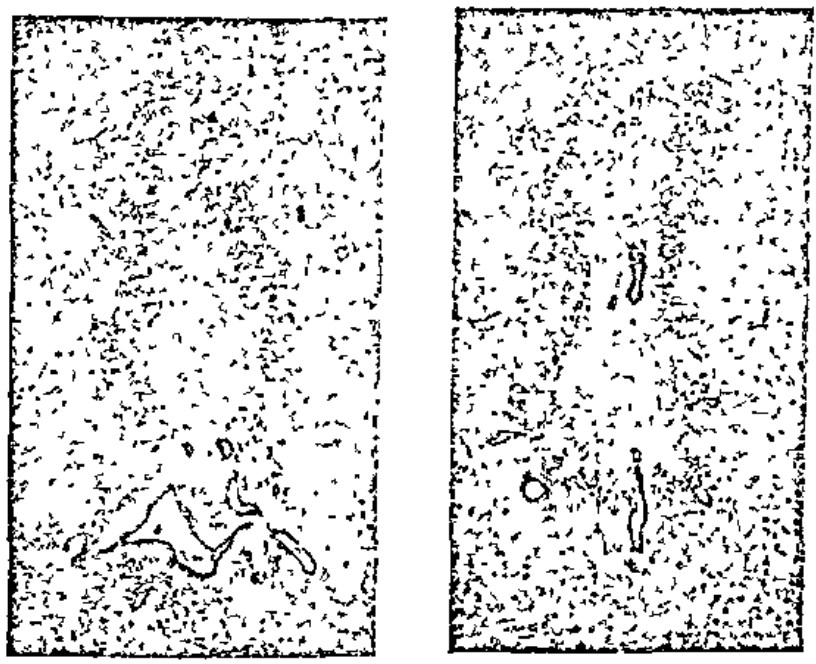


FIG. 23: *Case 24:* Transverse sections through the aqueduct at anterior (left) and posterior (right) levels, showing sub-division of lumen. The original contours of the aqueduct are represented by a zone of ependymal cells. H. and E. × 25

The interpretation of this case presents certain difficulties. The onset of the hydrocephalus a few days after birth suggests a basis in maldevelopment, and the case was at first regarded as an example of "forking". The microscopical identification of two main sets of ependymal channels in a dorsi-ventral relation to one another supported such a view. But the progressive nature of the hydrocephalus clinically, combined with the minute size of these channels at the time of death, suggests that the narrowing of the aqueduct was also progressive. The chief histological evidence for this is the remarkable zone of

isolated ependymal cells maintaining the normal outlines of the aqueduct, an appearance not so far seen in true "forking". Further the dorsal and ventral channels are separated by fibrillary glia, and not by normal neural tissue, a diagnostic point on which stress has already been laid. In parenthesis, the association of a spontaneous ventriculostomy in the left lateral ventricle with cessation of the expansion of the skull in the last two months of life is a matter of interest that will be considered in a later section (p. 127).

The case next to be reported lends some support to the interpretation which has been offered in respect of the first.

Case 25: F.B., male aged 5 years (Reg. No. 12374/1937). He was the third child of his parents, the other two siblings being alive and well. Birth took place at full term by forceps delivery. He weighed 9½ lb. Health was good until 7 months before admission when he began to be drowsy and to complain of headaches. More recently there had been attacks of unconsciousness accompanied by stiffening of the limbs and retraction of the head. He tended to fall backwards and to the right. Shortly before admission to hospital, and while under observation in the wards, he had frequent attacks of effortless vomiting.

On examination: He appeared a well-nourished and well-developed child with an enlarged head, measuring 51 cm. in circumference, which gave a cracked-pot note on percussion. There was early papilloedema, but visual acuity was good and the fields full. There was slight bilateral ptosis and generalized weakness of all limbs, with slight ataxia of the lower extremities. Radiography of the skull showed internal hydrocephalus. Lumbar puncture yielded clear fluid under a pressure of 140 mm. Death took place during exploration of the cerebellum.

Summary of necropsy: (P.M. 315/1937): *Infarction of lung from wax embolus: Internal hydrocephalus: Stenosis of aqueduct.*

Plug of bone-wax, corresponding in diameter to large emissary vein communicating with left lateral sinus, riding second bifurcation of pulmonary artery to lower lobe of right lung. Haemorrhagic infarct in lower fringe of this lobe Oedema of lungs. No further significant changes in other organs.

Brain: There was gross dilatation of the third and lateral ventricles; the fourth ventricle was of normal size. The anterior part of the aqueduct was greatly dilated, measuring 0·45 by 0·4 cm. and tapered to a pinpoint lumen, about 0·05 cm. in diameter, immediately anterior to the fourth ventricle. Here the lumen was enclosed by greyish tissue stained in places by haemolysis due to the escape of small quantities of blood into the lateral ventricles when tapped at operation.

Microscopic examination: Sections through the aqueduct at the point of greatest narrowing show a minute circular lumen with well-defined margins which are devoid of ependyma and

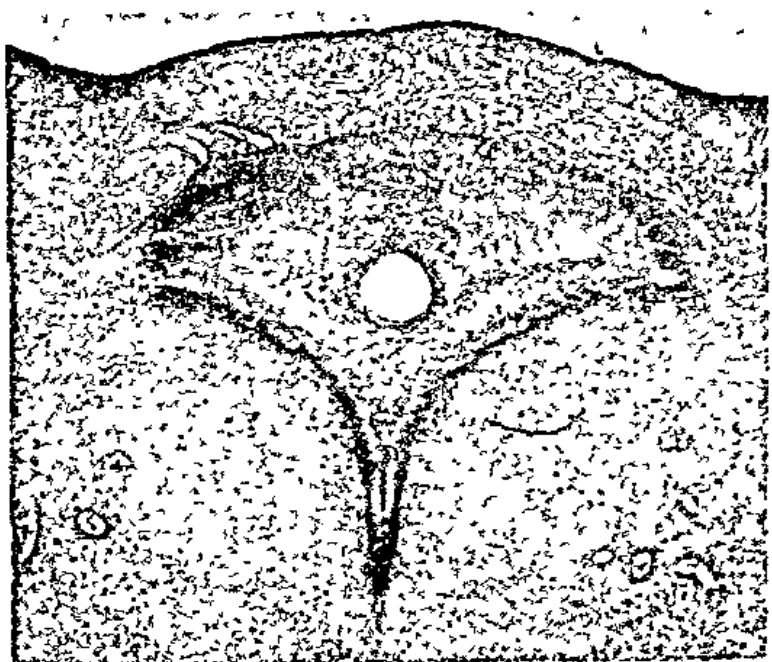


FIG. 24: *Case 25:* Advanced stenosis of lumen of aqueduct. The original, normal outline is seen as a dark zone (see text for description). Phosphotungstic-acid haematoxylin. × 14·5

composed of loose fibrillary glia. This glia forms an unbroken layer between the lumen and what appears to have been an antecedent lumen of normal size and shape (Fig. 24) The dark zone shown in the photograph is the densely fibrillary subependymal glia in relation to which are innumerable small groups of ependymal cells. It will be noted that the thickening of the glia is greatest over the dorsal region. There is no cellular inflammatory infiltration. A section immediately anterior to this, through the posterior corpora quadrigemina, shows the same general arrangement of tissue about a larger lumen ; the broken line of ependyma here takes the characteristic pear-shaped form of the aqueduct at this level. There is no alteration of the leptomeninges beyond focal extravasations of red corpuscles incidental to operative interference.

In this case both clinical history and pathological examination point to a progressive narrowing of the lumen of the aqueduct during post-natal life, the site being limited to the posterior extremity of this channel. The process is essentially a gliosis in which there is no clear evidence of inflammation. The ependymal cells do not participate but remain passively in their original situation, becoming rounded up into groups upon losing their contact with the lumen. There is nothing to show how or why this gliosis was initiated: possible theories will be examined after description of the remaining cases.

Case 26: G O'S., male aged 10 years (R.I 3722/1939) A full clinical description of this case is given by Pennybacker (1940) The child was apparently normal until three years before admission when he became clumsy with his hands One month before admission he began to have severe headaches with occasional bouts of vomiting

On examination he had a large head measuring 57 cm in circumference. There was bilateral papilloedema but no further neurological abnormalities beyond a vibratory tremor of the out-stretched limbs and a little unsteadiness on his feet. Radiography showed general enlargement, convolutional thinning, and separation of the sutures of the skull ; erosion of the sella was so marked as to suggest a lesion in its immediate neighbourhood. The cerebro-spinal fluid was normal

Ventriculography showed gross internal hydrocephalus, including the third ventricle ; the shadow of the aqueduct ended just beyond the third ventricle.

Death followed twelve weeks after ventriculostomy had been performed by splitting the lamina terminalis.

At *necropsy* (R I P.M 387/1939) no important changes were found apart from those in the brain The hole in the lamina terminalis was widely patent, and although the right Sylvian cistern was obliterated by post-operative adhesions, the left one and the cisterna basalis were ballooned, suggesting that the fistula had been effective. There was gross dilatation of the third and lateral ventricles, their lining being smooth and glistening The aqueduct tapered rapidly on leaving the third ventricle and appeared to be completely obliterated at the level of the hind border of the anterior corpora quadrigemina. The hind end of the aqueduct and the fourth ventricle were macroscopically normal.

Microscopic examination Transverse sections through various levels of the aqueduct show maximal disorganization of the lumen at the point of obliteration indicated by naked-eye examination. Here, as shown in Fig 25, the region is occupied by dense fibrillary gliosis embedded in which are a few canals, of varying calibre, lined with ependymal cells. A few macrophages containing iron pigment occupy one of the spaces. There is no inflammatory cellular infiltration of the adjacent glial tissue. Serial sections of the aqueduct from the point of maximal obstruction to the fourth ventricle show some degree of abnormality at all levels Passing caudally, the isolated groups of small channels seen in Fig. 25 gradually converge, forming the arrangement seen in Fig. 26. Here the lumen is surrounded by a zone of glial tissue which is less dense towards the centre than at the periphery. There is no ependymal lining, but the ependymal channels lie, in a disorderly fashion, at the margin of the zone of less dense glia At the level of the posterior corpora quadrigemina the aqueduct presents a normal pear-shaped outline, but its ependymal lining is extensively interrupted by numerous small cushion- and tongue-like nodules of glia which project into the lumen. There is, however, no excess of peri-aqueductal gliosis.

In the *fourth ventricle* there is pronounced subependymal gliosis at the dorso-lateral angle on one side, and at several places—mostly on the lateral walls—the ependyma is interrupted by shallow granulations of glial tissue.

The lateral wall of the *third ventricle* and the left occipital horn show considerable focal loss of ependyma, the lining being replaced by subependymal glia. In places there is cuffing of the blood-vessels of this layer with small lymphocytes, and occasionally a small group of foam-cells with one or two plasma cells adheres to the lining of the ventricle.

The *leptomeninges* at the base of the brain are infiltrated with a few polymorphonuclear leucocytes, lymphocytes and plasma-cells ; there is no fibrosis.

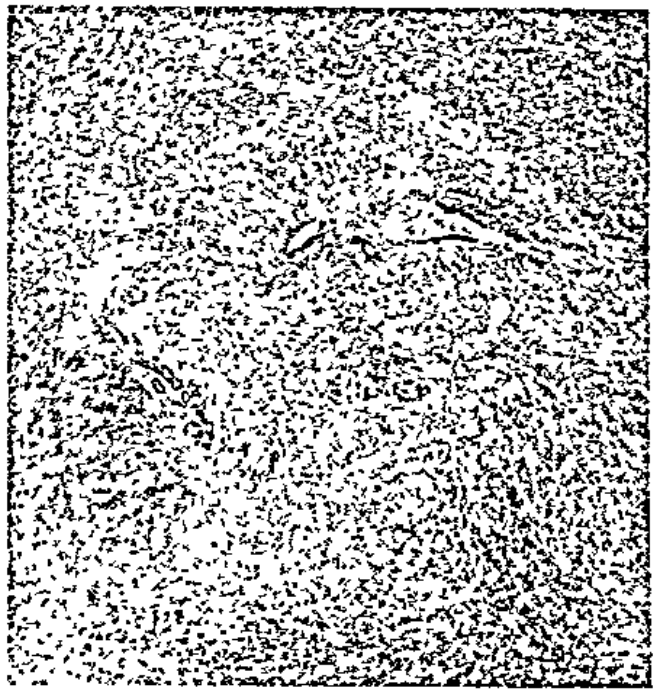


FIG. 25: *Case 26:* Site of aqueduct at level of A.C.Q The lumen is greatly sub-divided by gliosis. Phosphotungstic-acid haematoxylin. × 30

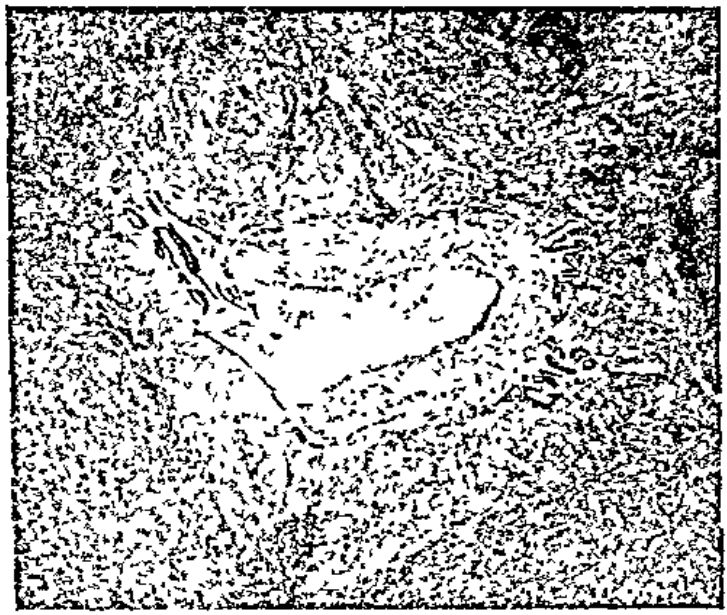


FIG. 26: A level posterior to that shown in Fig. 25. See text for description. Same stain × 30

From the combined clinical and pathological aspects this may be regarded as a classical example of gliosis of the aqueduct. Although an examination with the naked eye alone would suggest that the ependymal changes and gliosis were confined to the proximal part of the aqueduct, the microscope showed that this was not so. The whole length of the aqueduct was affected by an excessive granularity of the ependyma, while the fourth ventricle was similarly but less markedly involved. The low-grade ependymitis of the third and lateral

ventricles and the meningitis at the base of the brain were doubtless the result of operative interference: no inflammatory reaction of a similar kind was found in relation to the aqueduct or fourth ventricle. The appearances seen in the aqueduct just distal to the point of maximal occlusion (Fig. 26) suggest a progressive gliosis that is reminiscent of the two cases previously described. In the following case, the only one in the present series in an adult, there is further evidence that the pathological basis of this condition lies in a disorder of the ependyma that is not confined to the aqueduct but manifests itself at this point on account of anatomical considerations.

Case 27: I am indebted to Mr. Kenneth Heritage for the clinical history and pathological material relating to this case. G R., male aged 23. Occupation: labourer. He was quite well until November, 1939, when he began to suffer from morning headaches of increasing severity, followed, a few weeks later, by blurring of vision. Early in December he begin to feel unsteady on his feet, and had difficulty in walking straight. On January 1st, 1940, he was admitted to hospital. On examination visual acuity was greatly diminished (right, 6/24 , left, 6/36) ; the only other abnormal physical signs were bilateral papilloedema, coarse tremor of the outstretched fingers, and unsteadiness in walking, which was on a wide base Radiography of the skull showed digital impressions on the inner table of the skull, and erosion of the posterior clinoid processes. During observation over a period of two weeks there was deterioration in his mentality and he became semi-stuporose. His vision became worse and he developed a paralysis of the left sixth nerve.

On February 2nd ventriculography was performed. The cerebro-spinal fluid was under increased pressure, and gross dilatation of both lateral ventricles, and of the anterior part of the third ventricle, was demonstrated. The anterior end of the aqueduct was not identified The cerebro-spinal fluid contained 10 mg per cent. of protein. On February 5th the patient, after temporary improvement, relapsed into stupor and, to exclude the presence of a lesion in the superior vermis, a suboccipital craniotomy was performed, but the exploration was negative The patient survived for two days but, in spite of repeated ventricular taps, did not regain consciousness

Necropsy, limited to the brain, was performed 12 hours after death.

Examination of brain: *Macroscopic*. The specimen had been divided in the mid-sagittal

FIG. 27: *Case 27:* Mid-sagittal section of aqueduct showing occlusion beneath posterior corpora quadrigemina, and granulations in ependyma on both sides of this In the floor of the aqueduct the line of the original ependyma is seen as an interrupted row of dark dots. H. and E. × 6

plane after fixation in formaldehyde. The cut surfaces revealed an obstruction of the aqueduct beneath the posterior corpora quadrigemina through which it was impossible to pass a stout horse-hair. The quadrigeminal plate was not deformed, and the anterior part of the aqueduct was not obviously dilated. The fourth ventricle was of normal size. Dilatation of the third and lateral ventricles was less marked than that displayed by ventriculography, possibly because the central parts of the brain were soft and poorly fixed. The ependyma appeared normal save for diffuse haemolytic staining, due to slight intraventricular haemorrhage consequent upon operative procedures. The meninges appeared normal.

Microscopic examination: In longitudinal sections through the aqueduct (Fig. 27) there is a bridge of dense fibrillary glia extending across the lumen beneath the posterior corpora quadrigemina. It is devoid of ependymal cells except at its junction with the roof and the floor of the aqueduct, where small groups of these cells are aligned with the remainder of the ependymal epithelium. The ependyma of the aqueduct is, however, nowhere normal. Thus, anterior to the obstructing bridge, the floor is composed of a layer of fibrillary neuroglia completely overlying the ependymal cells. Deep to these cells the neuroglia is densely felted, and corresponds presumably to the zone of the original subependymal glia. In the roof of the corresponding part of the aqueduct, and throughout both roof and floor of the hinder part, the ependyma is interrupted by numerous granulations, and the adjacent neuroglia is conspicuously thickened. Beneath the anterior corpora quadrigemina the lumen is again narrowed by the approximation of roof and floor, and sections taken deeper from the paraffin block show that this narrowing is further increased by the projection of a shelf of fibrillary glia from the lateral wall.

The ependyma of both the third and fourth ventricles is interrupted by irregular granulations due to the inward irruption of the subependymal glia. No area examined showed infiltration with inflammatory cellular exudate.

This case strengthens the view, expressed in connection with the preceding one, that gliosis of the aqueduct is not merely a focal disturbance of the ependyma, but may more properly be regarded as the expression of a more widespread "ependymitis". The presence of ependymal granulations in the fourth ventricle is the best evidence in favour of this, since granularity of the ependyma in the dilated third and lateral ventricles may be interpreted as due to the hydrocephalus itself (see p. 119). In retrospect it is regrettable that fuller details are not available for the other cases. Future investigation will determine whether the observations made in the last two cases are significant or fortuitous. If significant, a further step will be gained towards an understanding of the ætiology of this disturbance.

Theories of Causation

In the meantime there is little agreement concerning the true nature of gliosis of the aqueduct. Some regard it as the result of maldevelopment and Spiller (1916) has argued that it is due to an excessive closing-in of the lumen such as may be seen in the thoracico-lumbar segments of almost any spinal cord. The histological result in both situations is sufficiently similar to render *this theory attractive. There is embryological support too, for the aqueduct is* undoubtedly of wider calibre in proportion to the brain-stem in the foetus than in the adult. Moreover, as Spiller points out, it is not unusual to find small groups of dislocated ependymal cells in the glia about the aqueduct in "normal" specimens selected at random. But against Spiller's theory is the excessive amount of fibrillary glia found in the region of the aqueduct in these cases of gliosis. Moreover, as already pointed out, two of the cases in the present series provide evidence of a widespread disturbance of the ependyma, involving the ventricles as well as the aqueduct. The same evidence makes it difficult to accept the neoplastic theory of gliosis of the aqueduct. To many pathologists this theory would be unattractive on histological grounds alone. Yet some hold that syringomyelia has a neoplastic basis, a condition in which the character of the glial reaction is similar. And it might be argued that some forms at least of granular ependymitis are of neoplastic origin in view of the

occasional finding of this condition in the central neurofibromatosis of von Recklinghausen. The following remarkable case is described in illustration of this point.

Case 28: N.J., a girl aged 11 (Reg No. 24063/1932). She was well until a few months before death when it was noticed that she squinted. At this time she developed frontal headache and occasionally vomited. On examination there was slight mental impairment with poor powers of concentration and lack of co-operation. The trunk was covered with flat pigmented areas of various sizes (Fig 28). There were no cutaneous nodules. Her head was slightly enlarged, measuring 52·5 cm. in circumference. There was bilateral papilloedema, most marked on the right. The pupils were equal and large, reacting poorly to light and

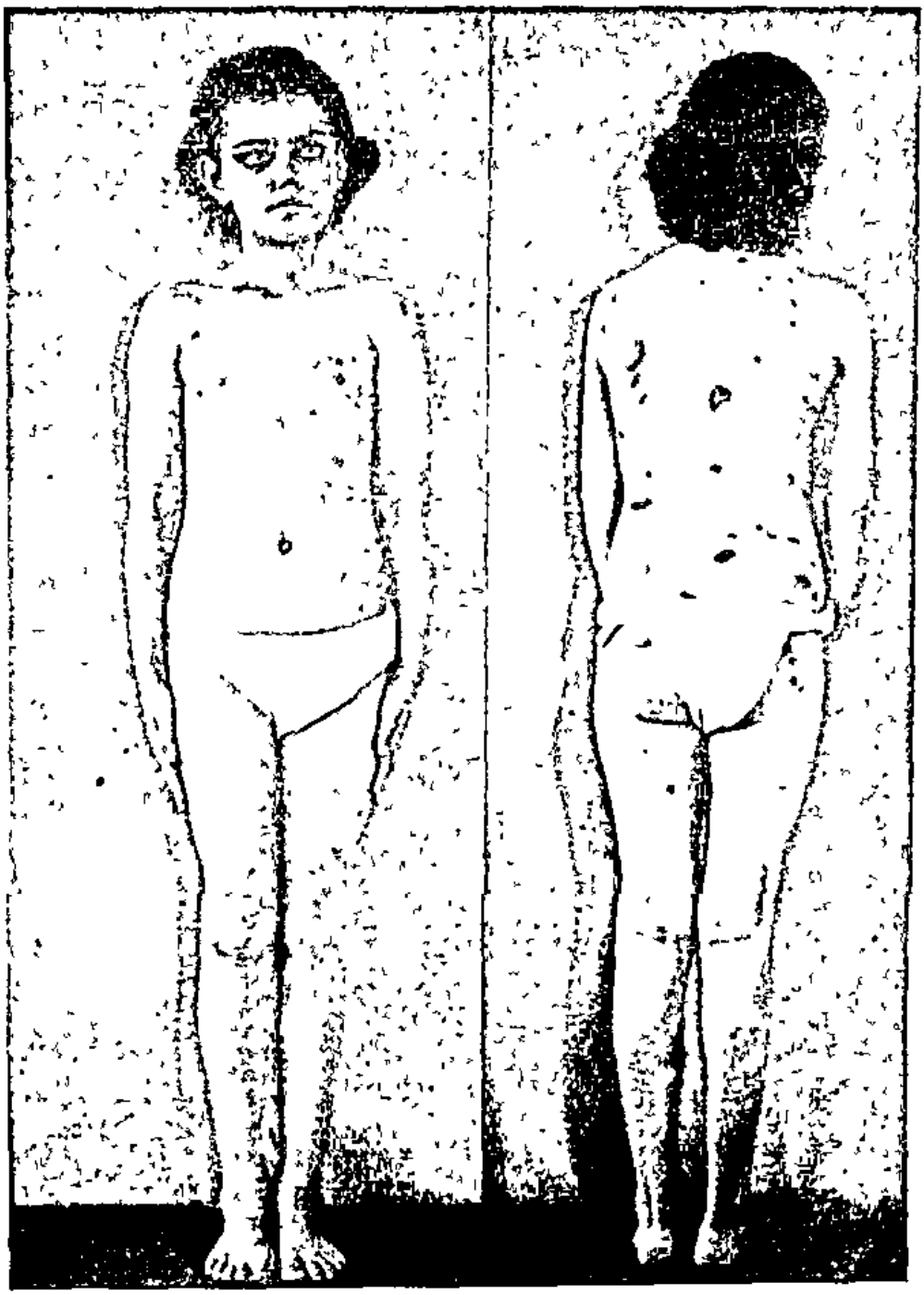


FIG. 28: *Case 28:* Note pigmented areas in skin

accommodation. There was bilateral weakness of the external rectus, especially on the right. No further abnormalities were noted in the cranial nerves. There was a generalized slight hypotonia with slight ataxy of the upper limbs and, after ventriculography, of the lower limbs. No sensory loss was observed. Radiography showed thinning of the vault with separation of the coronal suture. Wassermann reaction in blood negative.

Ventriculography The cerebro-spinal fluid was at a pressure of 600 mm. Bilateral symmetrical hydrocephalus with filling of the anterior half of the third ventricle was demonstrated

Craniotomy with exploration of the region of the pineal and upper surface of the cerebellum proved negative and the child died, some weeks later, without clinical improvement.

Family History: There were 17 siblings but none displayed any similar neurological or cutaneous abnormality.

Necropsy (P.M 595/1930) was limited to examination of the head and spinal cord.

Brain: The leptomeninges were normal apart from some residual areas of operative haemorrhage in the region of the cerebellum and base of the brain. The cerebral convexities were full and the convolutions flattened On median sagittal section the aqueduct was occluded at a point beneath the centre of the posterior corpora quadrigemina by a curved structure superficially suggestive of a septum (Fig 29). The adjacent ependyma was studded with granulations of pinhead and pinpoint size. A few similar granulations were also present in the fourth ventricle and in the ventral part of the third ventricle. The ventricular system anterior to the obstruction was grossly dilated.

Spinal cord: No abnormality was found apart from diffuse subarachnoid haemorrhage over its posterior surface.

Microscopic examination The obstruction in the aqueduct is composed of two granulations arising from the roof and floor respectively, which come into close apposition (Fig 30). They consist of sparsely cellular fibrillary neuroglia and are incompletely coated with ependymal epithelium A few clusters of similar cells are embedded in the substance of the ventral granulation There is no inflammatory cellular infiltration Numerous granulations are present in the dorsal part of the aqueduct anterior to the obstruction ; the floor is undulating but the ependyma here is intact. Similar granulations occupy the ependyma of the fourth and third ventricles. In the latter is a particularly large example measuring 4 mm The lateral ventricles contain relatively few granulations, and they are small and flat

FIG 29: *Case 28:* Granulations in wall of aqueduct

Extensive cutaneous pigmentation such as was seen in this case is a manifestation of von Recklinghausen's disease. But no obviously neoplastic process was identified in the central nervous system, unless the ependymal granulations are to be viewed in this sense. These were clearly the cause of the internal hydrocephalus. Such cases must be extremely rare, but Guillain (1935) has reported an instance, in a man of 30, in which hydrocephalus was associated

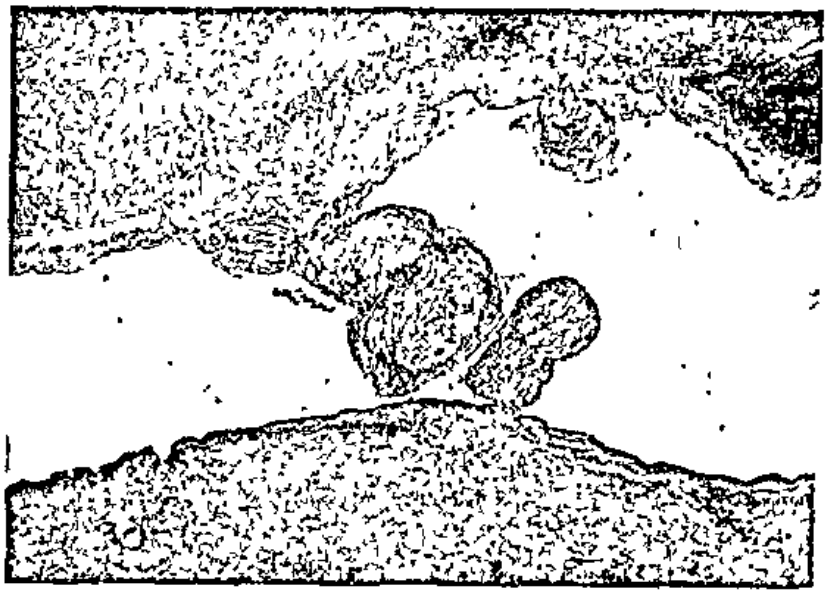


FIG. 30: *Case 28.* The approximation of polypous granulations from the roof and floor of the aqueduct obstruct the lumen. Phosphotungstic-acid haematoxylin. × 15

with ependymal granulations, which almost obliterated the aqueduct and considerably encroached upon the lumen of the third ventricle. Moreover, the right foramen of Monro was obstructed by a nodule, of the size of a pea, which projected from the ependyma and which resembled a polar spongioblastoma histologically. Though the ependymal reaction in these two cases may be of a neoplastic character, it will be shown later that granular ependymitis is certainly, and probably more commonly, an inflammatory manifestation.

We are led back therefore to the third possibility concerning the ætiology of gliosis of the aqueduct: namely, whether it may be an inflammatory process. There has been considerable support for this hypothesis in the literature, but on the whole little evidence can be found in its favour. Syphilis appears to play no part, though intra-uterine infection with resulting gliosis has been regarded as the responsible agent by d'Astros (1898) and others. The absence of inflammatory cellular exudate in the region of the ependyma and in the basal leptomeninges is against infection by bacteria or other organisms. On the other hand encroachment upon the lumen of the aqueduct by the subependymal glia without any accompanying cellular inflammatory exudate is sometimes encountered in cases of post-meningitic hydrocephalus (Case 41, p. 77). There remains the possibility that non-bacterial toxins circulating in the cerebro-spinal fluid may be responsible. The ependyma is apparently highly vulnerable and seems to have little, if any, power of regeneration. The subependymal glia, on the other hand, is capable of considerable proliferation when suitably stimulated. Hence it tends, in denuded areas, to protrude into the ventricular cavity in the form of granulations. Individual granulations may, as described later (p. 120), become confluent to form a complete investment over the remnants of disrupted ependyma. There are however no means as yet of proving whether such a process plays any essential part in gliosis of the aqueduct

CHAPTER IV

INFLAMMATIONS

THE meninges react to any foreign particulate matter circulating in the cerebro-spinal fluid, with the production of an inflammatory cellular exudate followed later, in many instances, by fibrosis. Although bacteria are the commonest cause of such a reaction, certain other non-bacterial agents deserve brief attention.

Exogenous Particulate Matter

Internal hydrocephalus has been produced experimentally in animals by the injection of substances such as aleuronate (Thomas, 1914), lampblack (Weed, 1920), trypan blue, or a mixture of potassium ferrocyanide and ferrous ammonium citrate (Wislocki and Putnam, 1921). The injections were made into either the ventricles or the cisterna magna. Young animals so treated may show expansion of the skull within ten days after the injection. The effect of these substances is to stimulate the arachnoidal cells lining the lepto-meningeal spaces. In their resting state the cells lie flattened out upon the connective-tissue framework bounding these spaces. When irritated, however, they become rounded and are shed into the cerebro-spinal fluid where they become phagocytes and are morphologically indistinguishable from polyblasts in other tissues of the body. After ingestion of the foreign particles they appear

FIG. 31: Large mononuclear cells filled with thorotrast granules in cerebellar leptomeninges (see text). P.M. 103/1937. H. and E. × 425

to lie dormant for an indefinite period, certainly for many months. Their ultimate fate has not been determined. The stages in this process of phagocytosis have been clearly described by Essick (1920). It is obvious that the conversion, on a large scale, of the arachnoid cells into phagocytes must lead to interference with the normal circulation of the cerebro-spinal fluid, especially when followed by the leptomeningeal fibrosis which forms a part of the inflammatory reaction.

In human subjects a similar reaction has been excited by the introduction into the ventricular system of "Thorotrast" (colloidal thorium dioxide) in ventriculography. The "Thorotrast" produces a chronic inflammation of the ependyma and choroid plexuses and, in the leptomeninges, a reaction of the kind described above. An early stage of this reaction is shown in Fig. 31, taken from the border of the cisterna magna of a woman suffering from a large cerebral glioma. A small volume of "Thorotrast" had been injected into a lateral ventricle 24 hours before death. Macroscopically, at necropsy, the appearances at the base of the brain suggested a slight focal purulent meningitis. As the photograph shows, the infiltration consists mainly of large mononuclear cells, the cytoplasm of which is stuffed with granules of "Thorotrast." The dangers of this substance, when used in this way, have been experimentally demonstrated by Stuck and Reeves (1938) at the Montreal Neurological Institute; they produced internal hydrocephalus in monkeys by introducing "Thorotrast" into the ventricles.

Endogenous Particulate Matter

Endogenous particulate matter can excite a similar meningitis, whether this is derived from the local breakdown of cells within the ventricles, from the extravasation on a large scale of red blood corpuscles, or from the storage within the arachnoid cells of abnormal metabolic products. The last-mentioned condition may accompany disorders of lipoid metabolism. It is well known that in Schüller-Christian's disease the meninges at the base of the brain and, in particular, in the region of the pituitary stalk, may be thickened by the deposition within macrophages of cholesterin esters and as a result of the associated inflammatory reaction. The dura mater is, however, principally involved and the literature does not provide any clear instance in which the cerebro-spinal pathway has been obstructed. Another variety of lipoidosis, akin to Niemann-Pick's disease and family amaurotic idiocy, is the condition of *Gargoylism*. In this the connective tissues of the body are widely involved in the storage of a complex myelin-like lipoid. This leads to clouding of the cornea and to thickening of the periarticular and other tissues. Enlargement of the head and internal hydrocephalus are salient features of the disease. The mechanism of the hydrocephalus has so far received no adequate explanation, mainly perhaps because few autopsies have been performed. According to Washington (1948) the enlargement of the skull is due to a defect in the mesodermal anlage of the top of the skull. In a case that came to necropsy at the London Hospital in 1938, and of which particulars have not yet been published, a different cause was found. The patient was a boy of nine years in whom the head was appreciably enlarged, measuring 58 cm. (Fig. 32). There was diffuse greyish-white opacity of the leptomeninges over the cerebral convexities and, less marked, at the base of the brain. In many places over the convexities the dura and arachnoid membranes were united by delicate fibrous adhesions. The foramina of Magendie and Luschka were patent. A conspicuous degree of external hydrocephalus was present, especially over the temporal poles and between the frontal lobes where clear fluid formed cystic collections indenting in places the adjacent brain which however was not atrophied. Fig. 33 shows some of these cystic spaces in the Sylvian fissures and also the considerable degree of internal hydrocephalus. Microscopical examination revealed fibrous thickening of the leptomeninges. The arachnoid cells contained small granules of material that was stainable

with Loyez' haematoxylin: an affinity shared by the lipoidal material stored in the neurones and other sites in the tissues. This storage was accompanied by *sparse cellular infiltration with lymphocytes and polymorphonuclear leucocytes.*

FIG. 32: Case of "gargoylism" in male, aged 9, showing enlargement of head

It thus appears to have initiated a low-grade inflammatory reaction with fibrosis of the leptomeninges and consequent obstruction of the cerebro-spinal pathway, especially at the outlets from the cisterna basalis.

The reaction excited by *haemorrhage into the leptomeninges* is of considerable

importance in relation to the pathogenesis of internal hydrocephalus. This reaction has been demonstrated experimentally by Bagley (1929) in dogs. Repeated small injections of the animal's own blood into the cisterna magna resulted, after a period of two months, in ventricular dilatation which was accompanied by fibrosis and matting of the leptomeninges, together with an infiltration with pigment-containing macrophages. In human pathology the most important implication is in connection with birth-trauma. While the severe and fatal intracranial haemorrhages associated with tears of the tentorium and of the great vein of Galen are familiar to all, the lesser, non-fatal haemorrhages that may pave the way for trouble at later stages are less fully

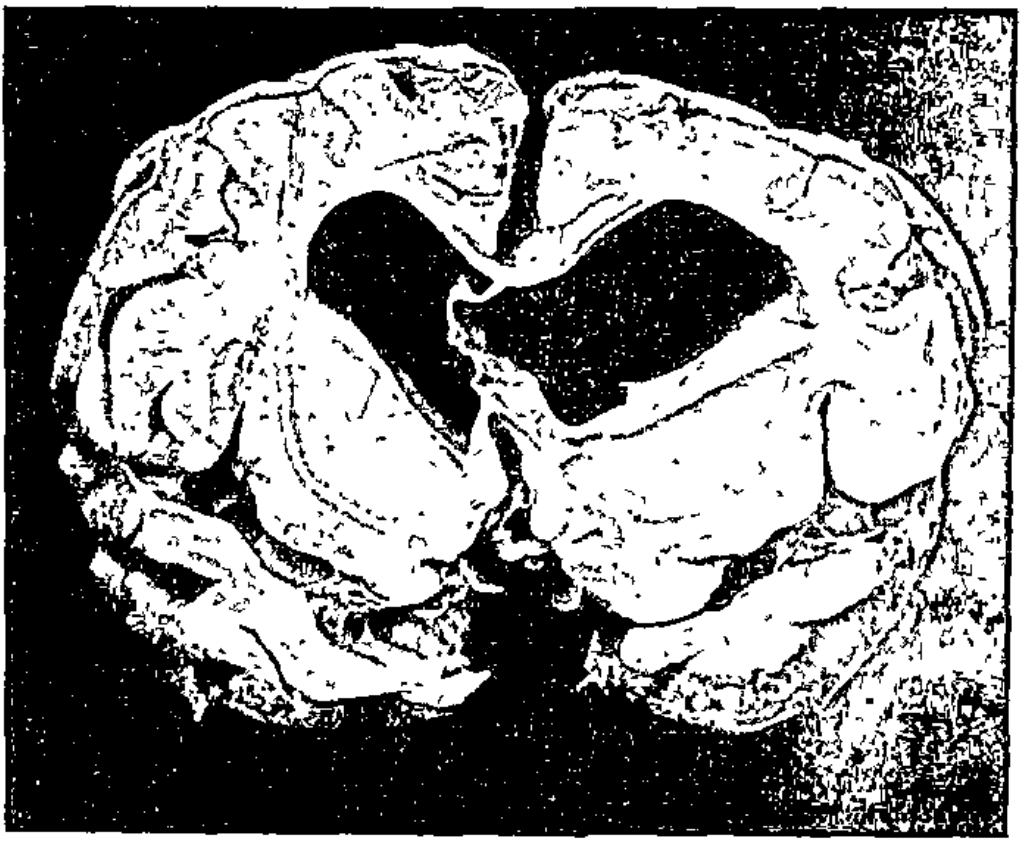


FIG. 33: From same case as in Fig 32, showing ventricular dilatation and cystic spaces in meninges of Sylvian fissures

appreciated. Their incidence is controversial: thus Sharpe and Maclaire (1924), performing routine lumbar punctures on a consecutive series of 100 newborn infants obtained blood-stained fluid in 13, of which 8 (of 51 cases) were first-born. Parsons (1944), however, does not accept the finding of a few red cells in the cerebro-spinal fluid, or even its yellow discoloration, as proof of haemorrhage ; he regards these abnormalities rather as evidence of "traumatic cerebral asphyxia". However that may be, it is not disputed that the premature infant is more prone to traumatic haemorrhages than the infant born at full term. In particular there may be bilateral haemorrhages, as described by Rydberg (1932), from the vein of the corpus striatum which may rupture into the lateral ventricles. A remarkable example of this lesion is illustrated in

Fig. 34. The section was prepared after fixation of the brain and evacuation of the blood-clot from the lateral ventricles which were greatly distended thereby. The specimen was obtained from one of *premature twins, each* weighing a little over 2 lb. and displaying the same condition of the brain. Over each vein of the corpus striatum, in the body of the lateral ventricle, was a circumscribed haemorrhage raising the ependyma. The physical basis of this type of haemorrhage is at present unknown. It might be argued that some strain upon the great vein of Galen caused back-pressure congestion in

FIG. 34: Horizontal section of brain from a premature stillborn infant showing bilateral subependymal haemorrhages from veins of corpus striatum (P.M. 100/1939)

the region of the basal ganglia and the rupture of these superficially placed veins. There is clear evidence that such ependymal haemorrhages can occur *in utero*. An example (P.M. 218/1931) was observed at the London Hospital, in an infant which survived Caesarean section for thirty minutes only, in which a haemorrhage from the vein of the corpus striatum was found. This haemorrhage must have occurred *in utero* because the area, on microscopic examination, was found to be crowded with macrophages containing iron pigment. The mother suffered from myxoedema and diabetes mellitus. Similar evidence is available from the report of Palmer (1928) on the causes of foetal death in a series of 144 cases. In his Cases CXI and CXII intraventricular haemorrhage was found and the foetus had apparently died before labour. The haemorrhages therefore

could not be attributed to pressure upon the head. Maternal eclampsia had been present in both instances and it was considered that either asphyxia or toxaemia were factors especially favourable to the haemorrhage.

Again Rydberg (1932) stated that in some of his cases with small intracranial haemorrhages the foetus had died *in utero* before any mechanical trauma was possible. In one example, obtained by Caesarean section before the onset of labour, death from mediastinal haemorrhage occurred on the fifth day and necropsy showed a small subdural haemorrhage in addition.

Toxaemia is regarded by Cruickshank (1930) as an important factor in the intracranial haemorrhage of infants. Both he and also Levinson and Saphir (1933) find that it is most prevalent amongst the prematurely born.

Fraser and Dott (1922-23) accept birth haemorrhage as a cause of infantile hydrocephalus. In seven, out of twenty-one of their cases of infantile hydrocephalus, there was a history of difficult labour and operation revealed the presence of haemorrhagic effusion in the membranes at the base of the brain. In certain of these the effusion involved the roof of the fourth ventricle and had led to occlusion of the foramina. Maclaire (1925) described the clinical development of hydrocephalus in an infant eight weeks after delivery by breech presentation. During the first few days of life the infant had been gravely ill with hyperpyrexia, oculo-motor disturbances and muscular spasms. Repeated lumbar punctures yielded thick bloody fluid.

The three cases now described provide further evidence of the same kind. Two additional cases have already been reported (Northfield and Russell,

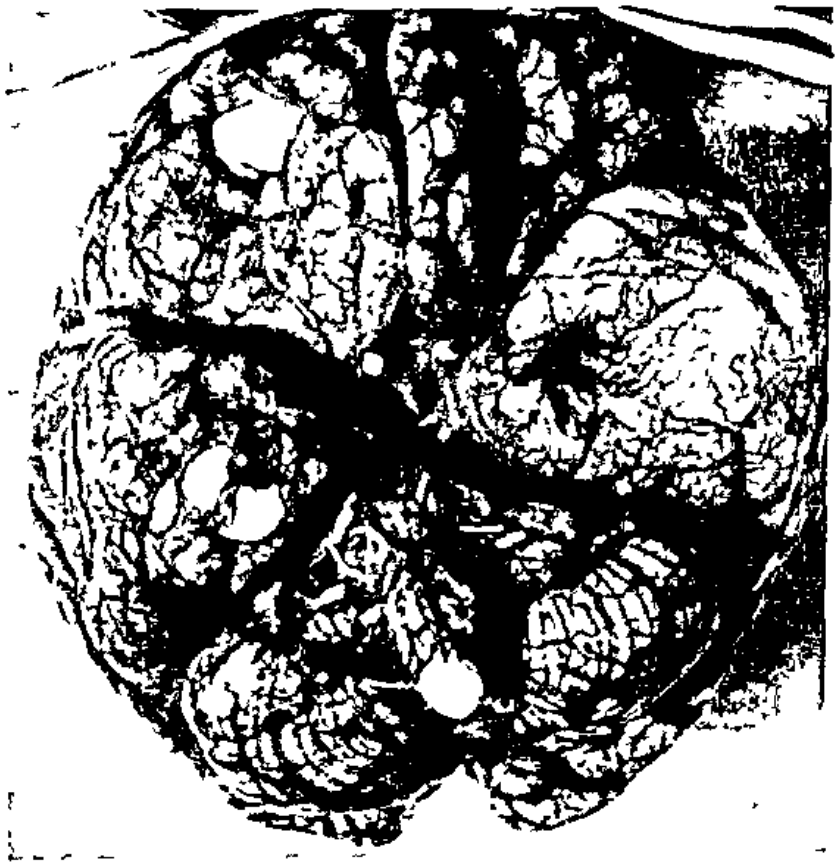


FIG. 35: *Case 29:* Base of brain showing distended left temporal lobe

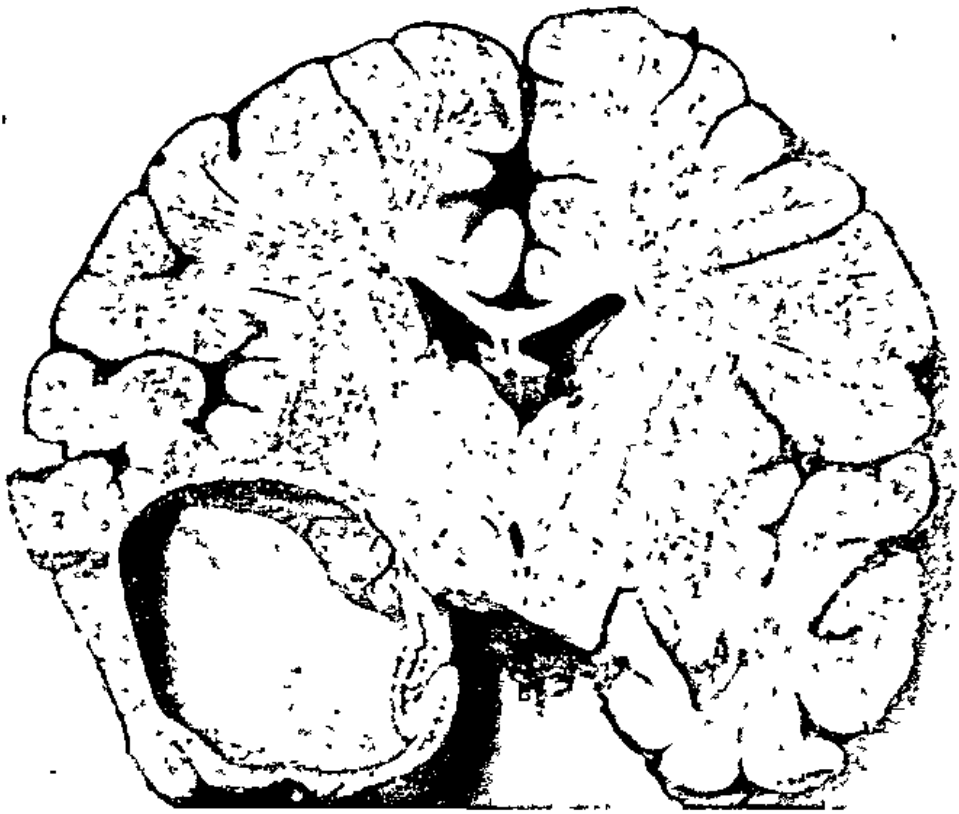


FIG. 36: Same case as in Fig 35: dilatation of left temporal horn

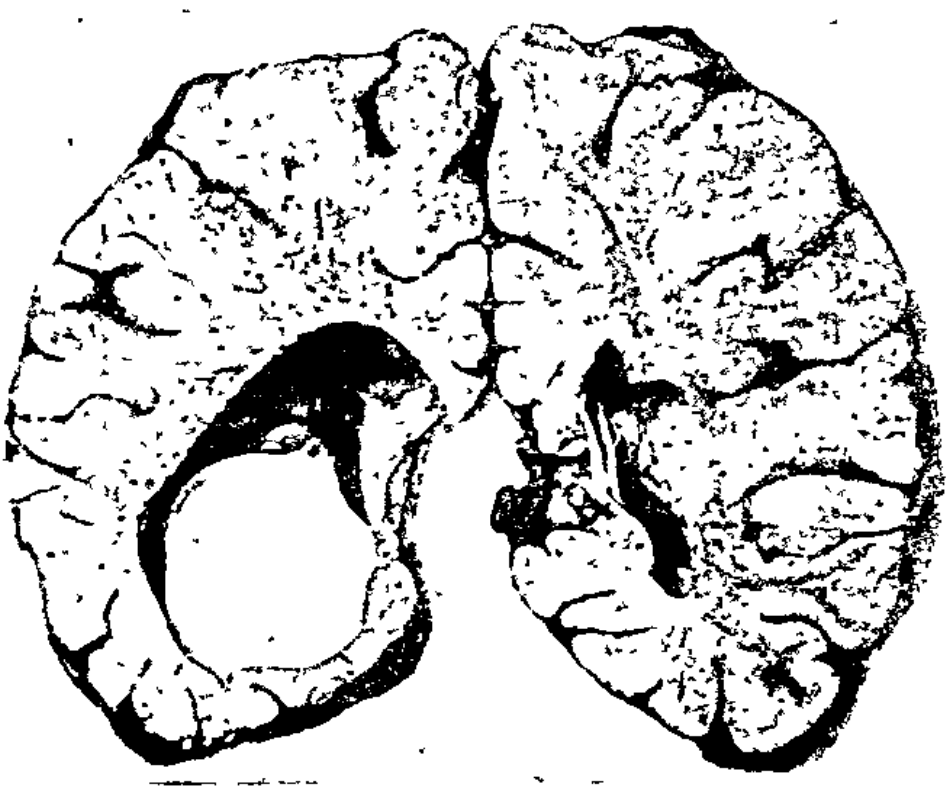


FIG. 37: Same case as in Figs. 35 and 36. The walls of the dilated left ventricle approximate round the choroid plexus (see text)

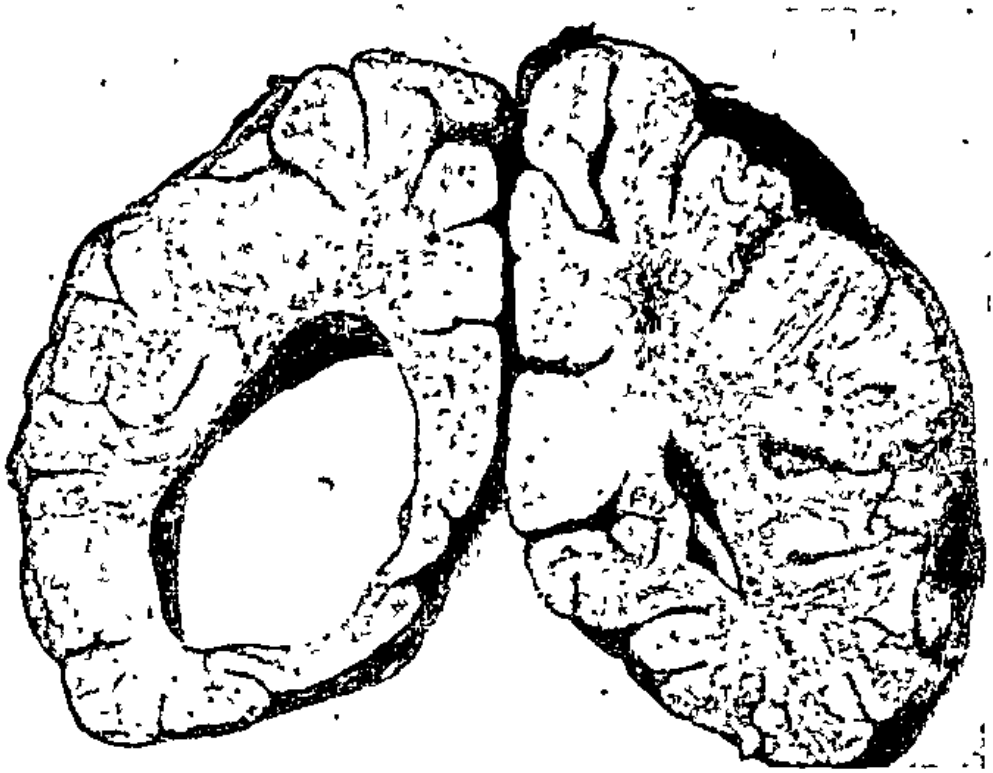


FIG 38: Same case as in Figs. 35, 36 and 37, showing dilatation of left occipital horn

1939): in these, chronic meningitis was due to diffuse meningeal haemorrhage and, in one of them, the history clearly indicated that the haemorrhage was due to birth-trauma.

Case 29. L.B., an infant aged 7 months (Reg. No. 31968/29, Med.). He was admitted to hospital with swelling of the neck, cyanosis and convulsions. Birth had been premature at 7½ months; the labour was normal; birth weight 4½ lb. There had been no illness until one week before admission when a slight cold developed.

Erysipelas of the scalp accompanied by a rise of temperature to 103° F. was manifest two days after admission and the infant died three days later.

Necropsy. (P.M. 2/1930). *Focal purulent meningitis over lateral aspect of right cerebrum Septicaemia. Cellulitis of face and right side of neck.*

The skull was conspicuously asymmetrical, the left middle fossa being greatly expanded, while the left anterior fossa was slightly smaller than the right. There was great cystic dilatation of the left temporal lobe without visible alteration of the adjacent leptomeninges (Fig. 35) On section this was found to be due to gross expansion of the left temporal and occipital horns, as illustrated in Figs. 36-38. At the posterior part of the body of the ventricle the roof was glued down to the fimbria by dense adhesions through which the choroid plexus passed by a pinhead meatus (Fig 37). The anterior part of the left ventricle and the remainder of the ventricular system appeared normal The ependyma everywhere was smooth and white. *Microscopically* the adhesions in the left ventricle are composed of collagenous and glial fibres, in the meshes of which are numerous macrophages laden with iron pigment. There is no inflammatory reaction and the choroid plexus appears normal.

The conspicuous unilateral hydrocephalus in this case was due to occlusion of the body of the left lateral ventricle by adhesions which appear to have had their basis in a focus of antecedent haemorrhage. The site corresponds to that in the lesions of the vein of the corpus striatum sometimes observed in the new-born (see p. 55). The fact that the infant in this case was born prematurely lends support to this interpretation. A similar localized form of hydrocephalus has been observed by Cairns *et al.* (1947) following penetrating wounds of the lateral ventricle. In the case now to be presented a symmetrical

hydrocephalus followed intracranial haemorrhage, apparently from both veins of the corpus striatum.

Case 30: D.S., a male infant aged 6 months (Reg. No. 13741/1932). He was admitted to hospital on October 20th, 1932, on account of progressive enlargement of the head. He had been born by breech presentation prematurely at 8 months, without the use of instruments. He appeared normal until 1 month after birth when abnormal enlargement of the head was observed. No other symptoms were noted.
On examination there was great expansion of the cranium which measured 60·5 cm. in circumference. No other abnormal physical signs were elicited. On October 24th, 10 c.c. of indigocarmine were injected into the left lateral ventricle. The dye was recovered 2½ hours later both from the right ventricle and by lumbar puncture.
Encephalography: Air injected by the lumbar route ascended to the base of the brain but did not reach the cerebral convexities; it appeared to be held up in the cisterns over the pons and optic chiasm. The child died on November 5th, 1932.
Necropsy: (P.M. 476/1932): *Multiple infarcts in lungs: Thrombosis of cavernous sinuses.* No significant changes in other organs. No abnormality of epiphyses in rib and femur.
Brain: There was slight yellow pigmentation of the dura near the olfactory grooves and the middle fossae, and a more conspicuous deposition was present over the clivus. Delicate fibrous adhesions united the dura to the arachnoid membrane over the cisterna magna. A patch of orange-brown thickening was present in the arachnoid membrane over the dorsal part of this cistern, and over the whole of the ventral surface of the brain the leptomeninges were thick, gelatinous and orange-brown. A similar alteration of the meninges was found over the adjacent cerebellum, the corpora quadrigemina and the proximal parts of the Sylvian fissures. On section the whole of the ventricular system was dilated, the lateral ventricles being most affected. The cerebral substance was reduced to a thickness of 2·5 mm. in the occipital region and 3·5 mm. on the medial aspect of the frontal lobes. The ependyma over either vein of the corpus striatum showed a patch of golden-brown pigmentation, that on the left measuring 3·5 by 1·7 cm., on the right 2·8 by 1·4 cm. There was slight yellow staining of the choroid plexuses in the third, lateral and fourth ventricles. No visible abnormality was found in the veins of Galen. There was ballooning of the lateral recesses of the fourth ventricle over each foramen of Luschka.
Microscopic examination: The leptomeninges over the base of the brain are considerably thickened by an increase of spindle fibroblasts and collagenous fibres, and are infiltrated with neutrophil leucocytes, lymphocytes and, above all, with numerous large pigment-macrophages (Fig. 39). The greater part of the pigment gives the iron reaction. A few microscopic purulent areas are present in the meshes of the fibrosis, but contain no organisms in Gram preparations. Vertical sections through the pigmented patches in the lateral ventricles show disruption of the ependyma by somewhat flattened granulations. Deeper, in the plane of the main subependymal vessels, is an interrupted zone of large mononuclear cells the cytoplasm of which is laden with haemosiderin (Fig. 40). They often form dense cuffs around capillaries and small veins. Similar cells are sparsely distributed between this zone and the ependyma. There is no further inflammatory infiltration. The subependymal glia is considerably thickened. *The epithelium of the choroid plexuses contains numerous granules of iron* pigment, especially in those villi that are most exposed to the ventricular fluid. No changes were observed in the stroma of the plexuses.

The pathological features in this case collectively point to meningeal haemorrhage, and the resulting inflammatory reaction, as the cause of the hydrocephalus. The source of the haemorrhage was apparently the veins of the corpus striatum: the position and histological character of the bilateral lesions of the ependyma support this interpretation. The presence of blood in the ventricles at some stage during life is indicated by the pigmentation of the epithelium of the choroid plexuses. On the clinical side it may be noted that the prematurity of the infant, and the development of the hydrocephalus about one month after birth, favour the interpretation already offered.

A remarkably similar case, in a difficult breech delivery, is reported by Moritz and Wartman (1938; Case 3). The child died at eight years and necropsy revealed ventricular dilatation, adhesions in the posterior fossa and iron pigment disseminated throughout the leptomeninges.

The classical tentorial tear may enter the picture in hydrocephalus if it happens to be associated with subarachnoid haemorrhage, as in the following case.

FIG. 39: *Case 30.* Meninges over medulla oblongata showing chronic inflammatory infiltration and pigment-macrophages. H. and E. × 145

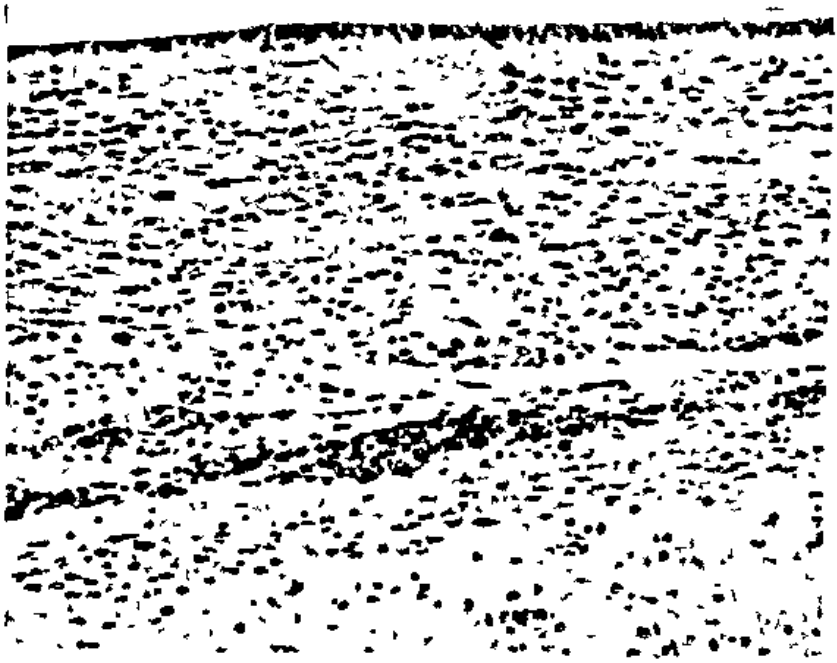


FIG. 40: *Case 30:* Site of subependymal haemorrhage in lateral ventricle showing zone of pigment-macrophages. H. and E. × 145

Case 31: L.B., a male infant aged 2 months (Reg. No 32966/1920). He was admitted to hospital three weeks before death suffering from vomiting, wasting and fits, of three weeks' duration. The mother had noticed expansion of the head for three days before admission. On examination the infant presented the hydrocephalic facies with the exposure of a broad rim of the sclerotic above the cornea. The anterior fontanelle was tense. Eye movements were dissociated; there was ptosis on the left side with a left internal strabismus. Right facial paralysis was also noted. Kernig's sign was positive and there was rigidity of the lower

limbs. Lumbar puncture on the day of admission, and again six days later, yielded blood-stained fluid. The Wassermann reaction in both blood and cerebro-spinal fluid was negative. There is no note about the circumstances of birth in this case, nor record of measurement of the skull.

Necropsy: (P.M. 487/1920): *Catarrhal gastro-enteritis. Intracranial haemorrhage.*

There was no evidence of injury to the scalp or skull. About 5 oz. of blood-stained fluid containing thin layers of gelatinous clot lay between the dura and the arachnoid. The inner surface of the dura was coated with a rusty red and grey membrane which was especially thick in the posterior fossa. A rupture (1·8 cm. long) traversed the left wing of the tentorium but did not enter its free margin. There was rusty pigmentation of the leptomeninges over the cerebellum and over the whole base of the brain, with slight fibrous thickening in the Sylvian fissures and the anterior end of the median fissure. Yellowish streaks of fibrin were found on the medial borders of the orbital surfaces of the frontal lobes. A few petechial haemorrhages were present in the cortex of the left frontal operculum and in the left upper temporal convolution. (The state of the ventricles was not noted.)

Though the data concerning this case are not as complete as could be wished, it is considered worthy of record since it provides an example of severe subdural haemorrhage with tentorial tear compatible with survival for two months. From personal recollection of this case hydrocephalus was a prominent feature clinically. But the expansion of the head may have been due in part to the subdural accumulation of bloody fluid.

A similar case has been reported by Coblentz (1940) in an infant of nine days. Labour had been uneventful and there was a moderate occipital caput. Enlargement of the head and bulging of the fontanelles were accompanied by slight cervical rigidity. Lumbar puncture produced grossly bloody, xanthochromic fluid. Ventriculography seven days later showed moderate symmetrical dilatation of the ventricular system and the ventricular fluid was slightly xanthochromic. A subdural encysted collection of blood was evacuated by cerebellar exploration and the infant recovered. It appears that the clot in this case impeded the escape and circulation of cerebro-spinal fluid in the posterior fossa.

Far less is known concerning the possible importance of meningeal haemorrhage in the production of hydrocephalus in the adult. No case occurs in the present series. Moritz and Wartman (1938) have however recorded three cases of this kind following head injury. Death followed the injury after 3½ months, 6½ months and 8 years respectively. Two cases were in young adults and one in a child of 4 years. A latent period elapsed between the injury and the onset of symptoms, which were mainly stiffness of the neck, lethargy, headache and vomiting. Necropsy revealed ventricular dilatation due to the blockage of the fourth ventricle foramina by adhesions. Deposits of iron pigment were present in the basal meninges.

An interesting case was recorded by Pye-Smith (1876) in a man of 35 who suffered from epileptic attacks beginning three years after a fall into a saw-pit, when his head was cut and he was "insensible and delirious for two days". His memory was defective on recovery. He died eight years later and, at necropsy, chronic hydrocephalus was associated with rusty pigmentation over the temporo-sphenoidal lobe, and similar spots over the under-surface of the frontal lobes. The aqueduct was patent. But it is stated that there were no signs of acute or chronic meningitis. Signs of a fracture were found in the postero-lateral part of the vault on the right. Although Pye-Smith attributed the hydrocephalus in this case to the results of trauma, it must be admitted that the anatomical evidence is defective. However it may form the earliest observation of this kind.

The "acute post-operative aseptic meningitis" described by Finlayson and

Penfield (1941) is of importance in this connection. The condition may arise after operations which involve opening the cisterna magna, or supratentorial operations which have left the ventricles widely open. Two of the patients in this report, dying from bronchopneumonia about 60 days after operation for removal of a frontal meningo-cerebral cicatrix, showed considerable internal hydrocephalus with chronic leptomeningitis and evidence of blood pigment in the tissues at the site of operation. Careful and repeated bacteriological examination of the cerebro-spinal fluid during life had failed to reveal any infective organisms. In experiments on cats these authors produced an acute aseptic meningitis by cisternal injections of fluid from a human subdural haematoma, fluid from a human cystic astrocytoma and, what is more significant, with autogenous sterile blood obtained from a week-old cerebral wound. The leptomeningitis in the human cases is thus plausibly attributed to the blood or other fluids accumulating at the site of operation.

Infections

NON-BACTERIAL INFECTIONS

Certain lowly organisms such as *Monilia*, *Torula* and *Toxoplasma* may infect the central nervous system with a resulting meningo-encephalitis. Internal hydrocephalus results from sealing of the fourth ventricle foramina, or from meningitis in the posterior fossa, but is not of an order to attract clinical attention. The rarity of such infections in this country will excuse their not being considered here at greater length.

Cysticercosis is of greater importance in connection with hydrocephalus and is now known, from the work of MacArthur (1934), to be more prevalent in our midst than had previously been suspected. The cysticercus stage of *Tænia solium* may readily develop in man, and the embryos show a considerable affinity for the brain. While any part of it may be so affected, it is quite common for the ventricles or the leptomeninges to be involved. When the parasites die a chronic inflammatory reaction is set up with resulting ependymitis and granulomatous meningitis and it is this inflammation, with the consequent obstruction of the cerebro-spinal pathway, that causes the hydrocephalus. This sequence of events has been widely recognized by continental workers, who have studied large series of cases, and in particular by Henneberg (1912) who has given a full account of the pathology. It was supposed by Henneberg that the death of the parasite and the subsequent inflammatory reaction were due to attacks by micro-organisms, said to be present within the cyst. But the character of the reaction supports better the argument advanced by MacArthur (1934) namely, that the parasite dies after a variable period determined by the resistance of the host, among other factors, and then stirs up a foreign-body reaction in its neighbourhood. There is surprisingly little reaction while the cysticercus is still alive.

At the London Hospital five cases of cerebral cysticercosis have been examined. Two of these showed numerous cysts throughout the brain, but neither the basal meninges nor the ventricles were involved; there was no hydrocephalus. In a third case the fourth ventricle was almost occluded by a botryoid mass of living cysts; the ependyma and basal meninges appeared normal and there was no hydrocephalus. In the remaining two cases hydrocephalus was present and they will therefore be briefly summarized.

Case 32: M.P., male aged 28 (Reg. No. 10633/1921, Surg.). The patient was admitted to hospital on account of headaches and vomiting, and died on the same day. He had been born in Poland but had lived in London for the previous 9 years. He had been investigated medically 6 months before death on account of vomiting, and a laparotomy had been performed. At that time members of the nursing staff had noticed that both his mentality and gait were peculiar.

Necropsy: (P.M. 95/1921): *Advanced internal hydrocephalus: Cysticerci occluding posterior half of fourth ventricle.* No cysts observed in other tissues.

There was great expansion of the lateral, third and anterior part of the fourth ventricles. The aqueduct was greatly dilated, measuring 0 8 cm. in diameter. A cyst, with lemon-tinted areas in its walls, occupied the hinder part of the floor and the left lateral recess.

Microscopic examination In two sections taken through the floor, and one through the roof of the fourth ventricle, the ependyma shows much disruption and is lost from many areas. There is severe gliosis in the floor, especially towards the lateral recess, and in one area this glia includes a small space containing eosinophil granular material. About this is a layer of multinucleate giant-cells enclosed by collagenous fibres. Surrounding this again is a zone of infiltration with lymphocytes, plasma cells and eosinophil leucocytes. A similar inflammatory reaction is present in a large part of the ventricular lining.

Case 33: S.D., male aged 35 (Reg No. 12544/1937). The patient had served with the Army in India, Egypt and Mesopotamia. For 10 years before admission to hospital he had suffered from right-sided Jackonsian attacks and, more recently, hemiparesis. During the 10 months before admission he had had attacks of headache and vomiting accompanied by aphasia, and loss of memory and libido

On examination there was evidence of increased intracranial pressure, dysphasia, right lower facial weakness and a right-sided spastic paresis Lumbar puncture yielded clear cerebrospinal fluid under a pressure of 220 mm , containing 40 mg of protein per cent. and 57 white cells, most of which were lymphocytes Radiographic examination of the skull revealed disseminated flecks over the surface of the brain, suggestive of cysticercosis. Ventriculography showed gross internal hydrocephalus. On cerebellar exploration the foramen of Magendie was found to be obstructed and efforts to relieve this obstruction failed. The fourth ventricle was opened through the vermis and found to be greatly dilated

Following operation there was a temporary improvement Two weeks later 3 c c. of methylene blue were injected into the left ventricle No dye was recovered from the lumbar fluid 1 hour later and, after 12 hours, it was still colourless though the ventricular fluid, at the same time, was tinged blue. Death took place on the following day

Necropsy: (P M 321/1937). *Internal hydrocephalus Cysticercosis of brain* No cysts present in other tissues. *Bronchiectasis of upper lobe of left lung*

The brain showed great internal hydrocephalus involving all ventricles, the ependyma being stained a faint blue from the injection A cerebellar pressure-cone, measuring 1 4 cm., was present. In all, 37 cysticercus cysts were identified in the brain and all, with the exception of one that was attached to the ependyma of the left occipital horn, showed stages of degeneration and calcification. One in the leptomeninges of the left Sylvian fissure had excited a focal inflammatory reaction resulting in the thrombosis of a main branch of the middle cerebral artery. Apart from this there was no visible meningitis The walls of the hinder part of the fourth ventricle were greatly softened and occupied by haemorrhage resulting from operation. The foramen of Magendie appeared sealed by fibrous adhesions and was impervious to water. No cyst could be identified in this region. There was an area of old softening in the left putamen and the adjacent internal capsule

Microscopic examination The left middle cerebral artery adjacent to the site of compression by the degenerating cyst shows organization and recanalization of a pre-existing thrombus. There is chronic focal arteritis of the segment abutting on the cyst The adjacent leptomeninges have undergone fibrous thickening and are infiltrated with small lymphocytes and plasma cells. There is a similar infiltration in the cervical dura and in the pia of the spinal cord. A late stage of descending pyramidal degeneration is present in the right side of the cord.

In this case internal hydrocephalus of a non-communicating type was due to closure of the fourth ventricle foramina by adhesions. Unfortunately no cyst was identified in this region, but the search was difficult on account of operative manipulations. There can be little doubt that the closure of the foramina resulted from inflammation caused by products of the degenerating cysticercus cysts in the brain. One such cyst was identified in the ependyma over the head of the left caudate nucleus.

The remains of a cyst were identified in the first case, and were associated with chronic ependymitis of the fourth ventricle. Sato (1904), in reviewing 128 cases of cerebral cysticercosis collected from the literature, found that the ventricles were involved by cysts in 48 instances. The fourth ventricle was

affected in 29, the cyst being solitary in 22 of these, the lateral ventricle in 16 and the third ventricle in 3 only. From this a predilection of the parasite for the fourth ventricle is clear, supposedly, according to Henneberg (1912), because the embryo gets into the cerebro-spinal fluid by way of the choroid plexuses and is carried down to the fourth ventricle foramina where it tends to get held up.

In none of our cases were the leptomeninges affected in the manner described by Hare (1938). In his two cases the base of the brain showed a yellowish or yellowish-grey exudate in the leptomeninges from the chiasma to the medulla oblongata, accompanied by marked internal hydrocephalus. The spinal fluid in his second case was under increased pressure and was cloudy, containing 6,500 white cells of which 66 per cent. were polymorphonuclear leucocytes. No organisms were found by films or culture. Histologically the meningeal infiltration was composed of lymphocytes, plasma cells, eosinophil leucocytes and large mononuclear cells. In both cases there were cysticercus cysts in the fourth ventricle with evidence of chronic ependymitis.

BACTERIAL INFECTIONS

In considering these infections in relation to internal hydrocephalus we are mainly concerned with the chronic bacterial forms of inflammation and with the sequelae of acute infections. In the early stages of an acute purulent meningitis the ventricles are usually small. Macroscopically the ependyma and choroid plexuses may appear normal, but histological examination of fulminating cases of pneumococcal meningitis has shown infection to be present at these levels within 24 to 48 hours of the onset of symptoms, and to be exciting the same tissue reactions here as elsewhere. Unless this phase is rapidly resolved it passes on to a stage of ventricular dilatation with pyocephalus. This is due to stagnation of the cerebro-spinal fluid within the ventricular system combined with progression of the inflammatory process. The stagnation is due mainly to two factors acting singly or in combination. The first, and commonest, is silting up of the fourth ventricle foramina and the outlets from the basal cisterns by the pus which forms in the leptomeninges and also drifts thither from the ventricles. The second is occlusion of the aqueduct by inspissated pus: a progressive change following purulent ependymitis and ending, in some instances, in organization of the pus by granulation tissue. At such late stages the ventricular fluid may again become clear, though its protein-content remains high, and the choroid plexuses and ependyma are, in variable degrees, disorganized by granulation tissue.

The following case illustrates this late phase of pyocephalus.

Case 34 E B, male aged 47. He was admitted to a military hospital for head injuries six weeks after a motor-cycle accident, in which he sustained an open compound and comminuted fracture of the frontal region involving the right orbit. In spite of local surgical treatment the wound became infected and there was clinical evidence of repeated waves of meningeal infection. Nevertheless he improved slowly. Lumbar puncture six weeks after the accident yielded yellow fluid at a pressure of 130 mm., containing 200 mg. of protein and 387 cells, of which 18 per cent. were neutrophil leucocytes and the rest lymphocytes.

X-ray examination showed, in addition to the fractures, a large aerocele in the substance of the right frontal lobe. Communication between this and the ventricle was demonstrated by the presence of a little air in the right lateral ventricle. An earlier skiagram, taken before admission, had shown no evidence of air in the brain. Treatment induced little change in the patient's condition and he died, a month later (*i.e.* 10 weeks after the accident), with further signs of meningitis and increased intracranial pressure.

Summary of necropsy. (R. I. P. M. 448/1940): *Chronic purulent meningitis: Infected traumatic aerocele of right frontal lobe: Head injury.*

The body of a greatly-wasted man. Right eye-ball greatly sunken, the upper lid being distended by a hernia cerebri, measuring 4 × 3 cm., and up to 2 cm. high, in the centre of which a minute fungus emitted small quantities of clear fluid. Comminuted fracture of right frontal bone, including orbital plate through which the cerebral hernia protruded. Dense fibrous adhesions between dura and right frontal pole in region of fractures. Slight broncho-pneumonic consolidation of lungs. Early pyelitis. Cystitis cystica of urinary bladder. No further abnormality except in the brain. Middle ears and accessory air-sinuses normal.

Brain: The right frontal lobe was swollen and fluctuant, and from it escaped a quantity of clear fluid during removal of the brain from the skull. The ventral surface of the frontal pole was firmly united to the dura over the cribriform plate and there was conspicuous orange pigmentation of the leptomeninges about this area, and also over the occipital poles. A little purulent exudate was present in the basal cisterns and over the inferior surface of the cerebellum. On section the frontal lobe contained a large cyst measuring 4 cm. in diameter and about 6 cm. antero-posteriorly, which communicated with the anterior horn of the ventricle beneath it by an oval aperture measuring 2·3 by 1 cm. (Fig. 41). This cyst had a firm, grey, glistening wall which blended anteriorly with the meninges. Its floor and lateral walls were coated with thick pus. The third and lateral ventricles were considerably dilated, the foramina of Monro enlarged and the grey commissure elongated. Both occipital horns contained thick grey pus and similar pus coated the choroid plexuses. The aqueduct was of normal size but its lumen was blocked with inspissated pus towards the fourth ventricle. The *fourth ventricle was undilated and empty apart from a little exudate over the choroid plexuses.*

Microscopic examination. The walls of the cyst in the frontal lobe are similar to those of a chronic cerebral abscess, the fibrous tissue layer being most strongly developed near the meninges, but poorly formed near the site of communication with the ventricle. The walls of the ventricles show a chronic purulent ependymitis which appears of more recent date than the inflammatory reaction in the wall of the cyst. The hind end of the aqueduct is blocked by disentegrating pus the borders of which show, in places, organization by young blood-vessels *and delicate collagenous fibres derived from the neighbouring subependymal vessels (Fig. 42).* The leptomeninges about the cisterna magna are infiltrated somewhat unevenly with neutrophil leucocytes and large mononuclear phagocytic cells; there is no appreciable fibrosis.

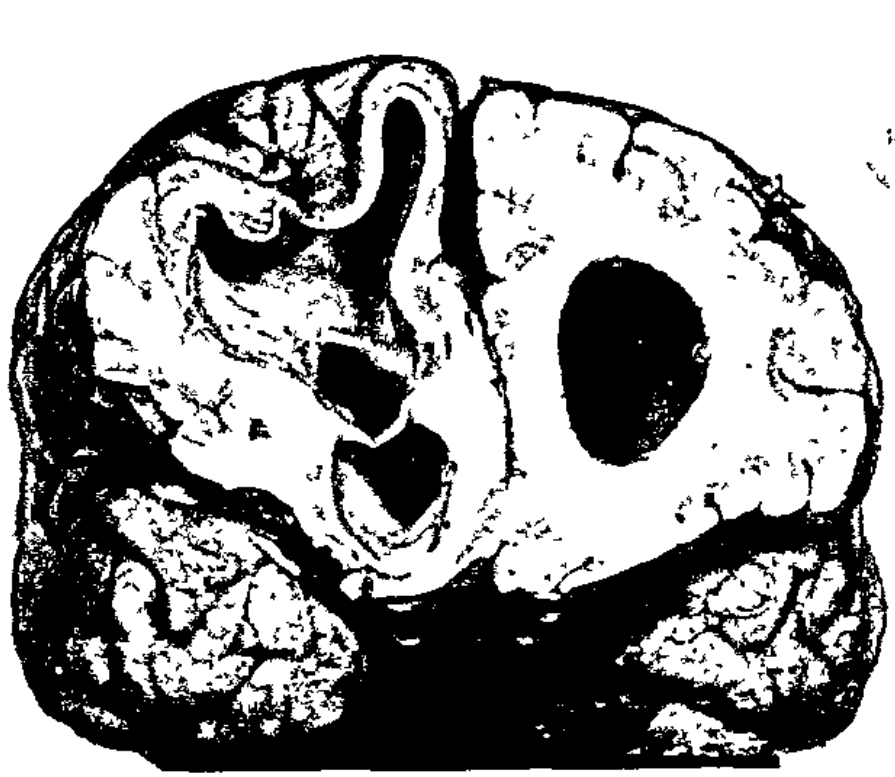


FIG. 41: *Case 34*: Traumatic aerocele in left frontal lobe communicating with frontal horn below

In this case it is clear that the cerebro-spinal pathway was infected by way of the traumatic aerocele which communicated secondarily with the ventricular system. A low-grade meningitis resulted, but microscopical examination

showed that it was blockage of the aqueduct rather than meningeal reaction that led to ventricular dilatation.

FIG. 42: *Case 34.* Border of aqueduct showing inspissated pus infiltrated with macrophages (top) and organization with formation of reticulin fibres (below) H. and E. (top); Foot's silver impregnation (below). × 185

Though chronic purulent meningitis cannot be considered a common cause of gross ventricular dilatation there are several examples of this sequence in the present series. All but one of these have been in infants. The following is an outstanding example.

Case 35: M.A.S., female infant aged 5 months (R.I. 28517/1944). Normal birth at full term (weight 5 lb. 4 oz.). Admitted to the Horton General Hospital, Banbury, at the age of 7 weeks with symptoms and signs of pneumonia. There was no neck rigidity nor other evidence of meningitis. After four days during which she was treated with sulphathiazole her condition had improved but, on discontinuing the drug, the temperature again rose (103° F.) and, six days later, the fontanelle was bulging. Lumbar puncture yielded 4 c.c. of turbid fluid.

On the following day (11 days after the onset of the illness) she was transferred to the Radcliffe Infirmary. On the supposition that the meningitis was due to pneumococcal infection the right lateral ventricle was immediately tapped and, after withdrawing 10 c.c. of turbid fluid, 7,000 units of penicillin were injected into the cavity and 30,000 units were given

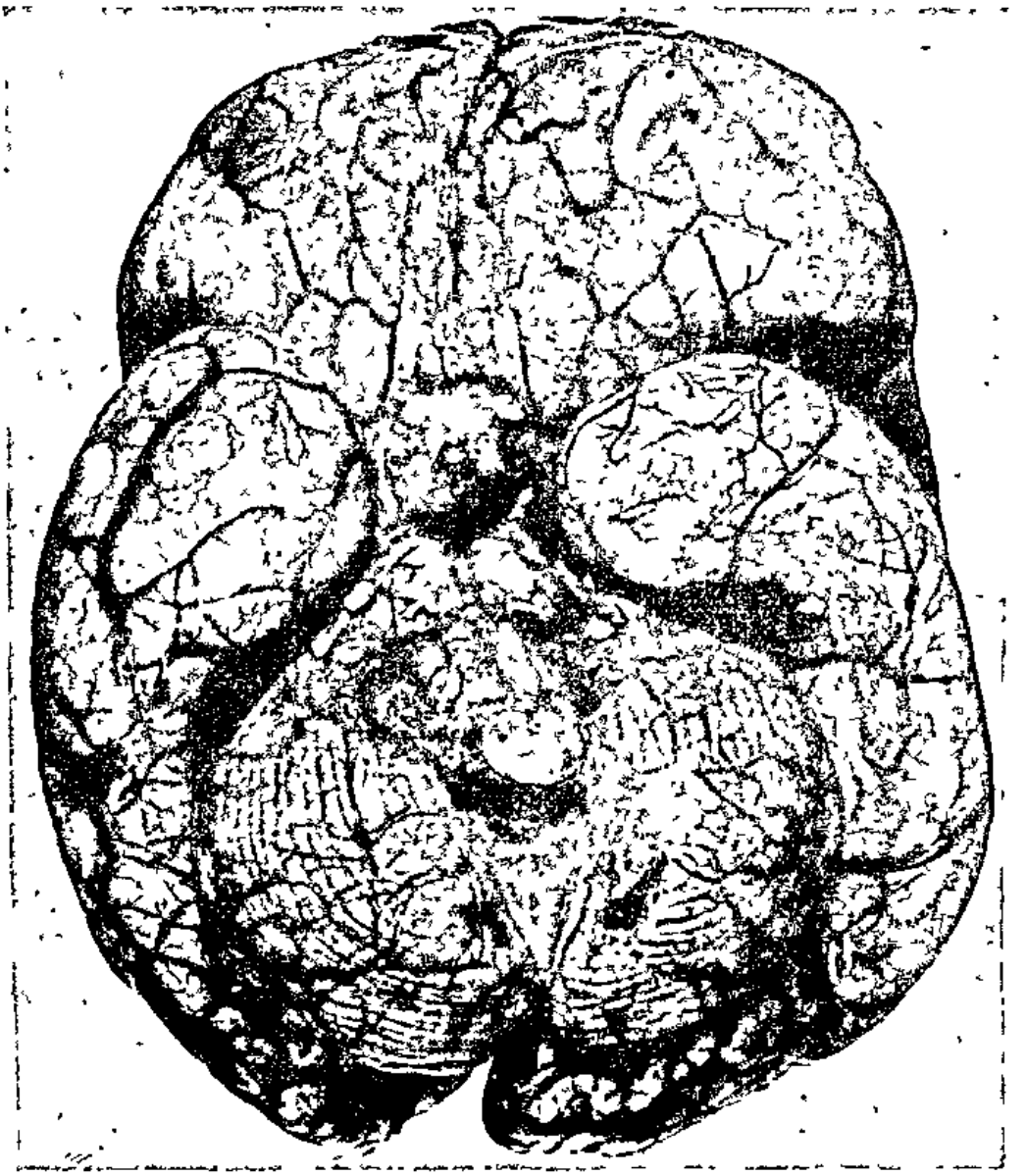


FIG. 43: *Case 35:* Base of brain showing purulent inflammation of meninges, especially in cisterna magna

intramuscularly. The circumference of the head at the time of admission was 39 4 cm.

The sample of ventricular fluid contained 140 mg. per cent. of protein, 4,500 red corpuscles and 310 white cells of which 70 per cent. were polymorphonuclear leucocytes and 27 per cent. lymphocytes. Films showed a moderate number of polymorphs and Gram-negative bacilli. Cultures yielded a growth of an atypical coliform bacillus. Thereafter the child received a course of sulphadiazine and improved for the next two weeks. This improvement however

was not maintained: the organism was found to be sulphonamide-resistant and, though some samples of cerebro-spinal fluid proved sterile, positive cultures were repeatedly obtained. Gradually increasing levels of protein (up to 1,000 mg.) and of the cell-content (up to 3,000) with predominance of polymorphonuclear leucocytes, were accompanied by gradual deterioration and expansion of the head. Ventriculography was performed on two occasions, two and three months respectively after the onset of the illness, and showed progressive dilatation of the ventricular system. Death took place 13 weeks after the onset of the illness.

Necropsy: (R.I. P.M. 454/1944): Apart from profound general wasting, pathological changes were confined to the central nervous system. The fontanelles were widely patent, especially the anterior. The cerebral convexities were dry, flattened and fluctuant, but devoid of exudate. The cisterna magna was ballooned by thick pus, its margins being apparently sealed off by fibrous adhesions (Fig. 43). Similar adhesions matted the meninges about the lateral recesses, the cisterna interpeduncularis and chiasmaticus. A few flecks of purulent exudate were present in sulci over the frontal poles. On section there was great generalized ventricular dilatation (Fig 44) accompanied by a collection of glairy greyish-green pus. The ependyma was thick, grey and succulent and was overlaid by a fine cobweb of glistening grey material. The aqueduct was also dilated and occupied by inspissated grey pus, with a resultant blurring of its outline. The fourth ventricle contained thick pus.

Microscopical examination: There is fibrous thickening of the leptomeninges at the base of the brain, especially about the foramina of Luschka and at the margins of the cisterna magna ; it is less marked around the mid-brain and rapidly fades away over the lateral lobes of the cerebellum. Large mononuclear phagocytes predominate in the cellular infiltration but are accompanied by plasma cells, small lymphocytes and fewer neutrophil leucocytes Large masses of necrotic leucocytes occupy the cisternal spaces, with an admixture of foam-cells as the meningeal borders of these spaces are approached. Similar pus fills the aqueduct and forms a layer over the walls of the fourth ventricle. The ependyma is disrupted into short strips and tubule-formations by an ingrowth of fibrillary neuroglia infiltrated with plasma cells and large mononuclear cells, and accompanied by proliferating blood-vessels cuffed with similar cells. This tissue gives place to an inner zone of denser infiltration, principally of plasma cells, supported by a delicate reticulum of collagen fibres and occasional capillaries. This granulation tissue is in direct contact with the free pus of the lumen, and is often coated with the large foam-cells which abound in the more peripheral parts of the pus.

In the lateral ventricles there is conspicuous subacute ependymitis shown by the cuffing of the subependymal vessels with plasma cells and lymphocytes, and by gliosis. But the surface ependyma, though frequently interrupted, maintains its normal marginal position

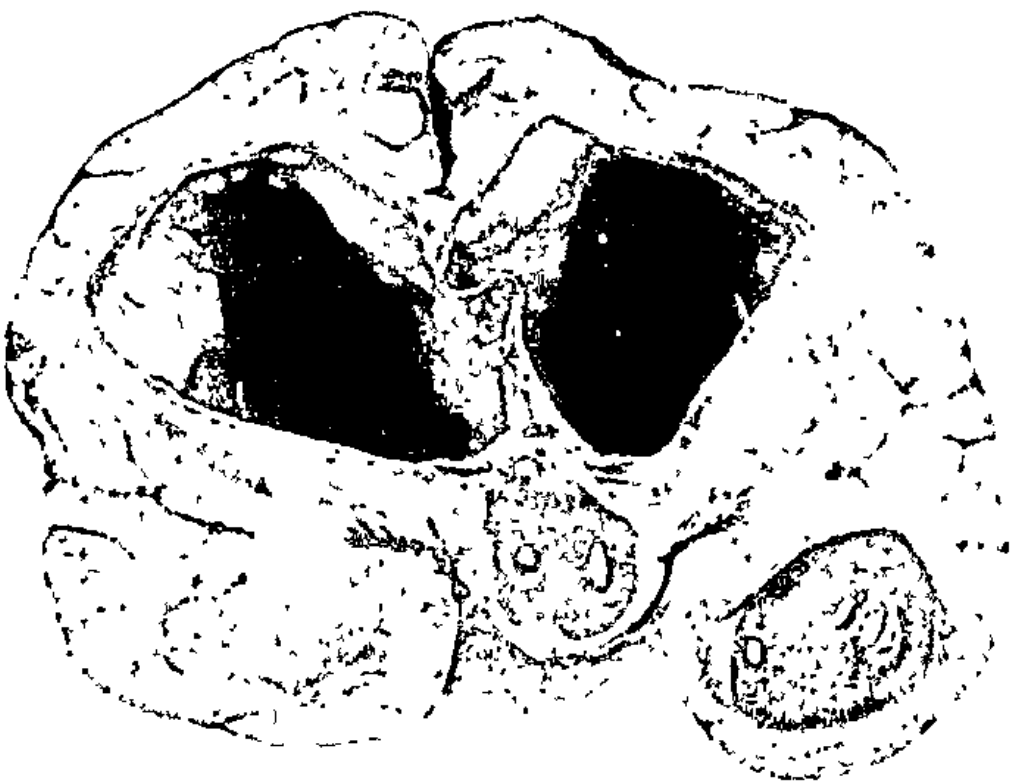


FIG. 44: *Case 35:* Dilatation of ventricles and pyocephalus

The generalized ventricular dilatation in this case suggested that the site of obstruction lay in the leptomeninges, and examination of the brain revealed thick inspissated pus filling the cisterna magna, while the remaining basal cisterns showed considerable matting by fibrous tissue. In addition there was obstruction of the aqueduct by inspissated pus and microscopical examination showed that stasis had been present at this level long enough to permit organization of the periphery of the plug. The dilatation of the aqueduct and fourth ventricle suggests that the intraventricular block arose at a later date and was therefore secondary to the meningeal obstruction.

The case thus shows that the clinical picture of internal hydrocephalus can complicate a purulent leptomeningitis due to an organism which excites a relatively low-grade inflammatory reaction, especially in young children with ununited sutures. While *Bact. coli* is, in general, a rare cause of purulent meningitis there is evidence that the newborn infant is susceptible. Cruickshank (1930) in an investigation of 800 neo-natal deaths in Glasgow found 33 cases of meningitis. In 10 of these the bacteriology was unsatisfactory. In the remaining 23 cases coliform bacilli alone were found in 11: streptococci (7), pneumococci (3), staphylococci (1), and *B. pyocyaneus* (1) made up the remainder. Thus *Bact. coli* was responsible for approximately half. Cruickshank hesitated to accept these figures at their face value, attributing some to postmortem or agonal invasion of the tissues. However, a more recent investigation of the same kind by Craig (1936) in Edinburgh establishes a similar incidence of infection by this bacillus. Out of 21 cases of neo-natal meningitis the organism was obtained in pure culture either from the meninges or from the spinal fluid in 10—again 50 per cent. of the total. In three further cases the bacillus was mixed with other organisms. In a series of 705 cases of meningitis in infants and children up to 12 years of age Fothergill and Sweet (1933) found the *Bact. coli* during life in the blood and cerebro-spinal fluid in nine cases in young infants. Further reference to these infections of infancy and their relationship to the chronic forms of meningitis found in the later years of childhood will be found in the discussion on p. 81.

In the following case internal hydrocephalus was secondary to a staphylococcal abscess of the cerebellum and chronic purulent basal meningitis in an adult.

Case 36: N.I, a woman aged 39 years (Reg. No. 23100 and 41928/1938) The patient was admitted to hospital complaining of sleeplessness for the preceding year and persistent headache for 6 weeks. She often vomited after food. For one week there had been dimness of vision and occasional diplopia.

On examination she looked ill and showed difficulty in concentrating but could answer questions slowly. There was slight bilateral papilloedema, the visual fields were full to rough tests and the ocular movements were full though there was slight bilateral ptosis. There was slight hypotonia of the left upper and lower limbs with weakness of abduction at the shoulder and of flexion at the elbow An extensor plantar reflex was obtained on the right. No further physical abnormalities were found until, a few days later, she developed skew deviation of the eyes, the left being higher than the right, and diminution of the left corneal reflex *On lumbar puncture* the pressure of cerebro-spinal fluid was 290 mm. with no evidence of block. It contained 120 mg. per cent. of protein and 785 cells, of which 65 per cent. were polymorphonuclear leucocytes and the rest lymphocytes. *Culture Staphylococcus aureus.* Lange curve: 1111342100 The *blood* showed a leucocytosis of 12,000.

Ventriculography showed a symmetrical hydrocephalus

She died three days after an operation for cerebellar decompression at which evidence of adhesive leptomeningitis was found.

Necropsy: (P.M. 496/1938): Was limited to examination of the head. The middle and internal ears on both sides contained a little clear blood-stained fluid. The meninges appeared normal except at the base of the brain. Here the arachnoid membrane over the pons and the cisterna magna was opaque, greyish-white and wrinkled. The cisterna magna was filled with

firm grey exudate while the left foramen of Luschka was obliterated by tough greyish-white granulation tissue containing soft grey exudate in its centre. In this region the leptomeninges were united by fibrous adhesions to the dura over a small area. Over the right foramen of Luschka the arachnoid was greatly ballooned (Fig. 45), its margins being firmly tethered down to the adjacent pia. On section an abscess, measuring 1·5 by 0·9 by 1·5 cm. from before backwards, occupied the ventro-lateral border of the left dentate nucleus, the adjacent cerebellar tissue being greatly indurated (Fig. 45). It did not involve the ependyma of the fourth ventricle but appeared to have spread to the meninges by way of the adjacent foramen of Luschka. The whole of the ventricular system was greatly dilated, the ependyma being everywhere smooth and glistening. Although the foramen of Magendie appeared to be closed it permitted water to escape slowly when tested after fixation.

Microscopical examination shows the abscess to be enclosed by a wall of young granulation tissue infiltrated with macrophages, plasma cells and lymphocytes. Nearby are a few similar smaller abscesses and, impinging on the meninges of the cerebello-pontine angle, there is an older abscess with a wall composed of dense collagen. The ependyma of the fourth ventricle shows subacute ependymitis. Purulent pachymeningitis is present in the dura over the clivus.

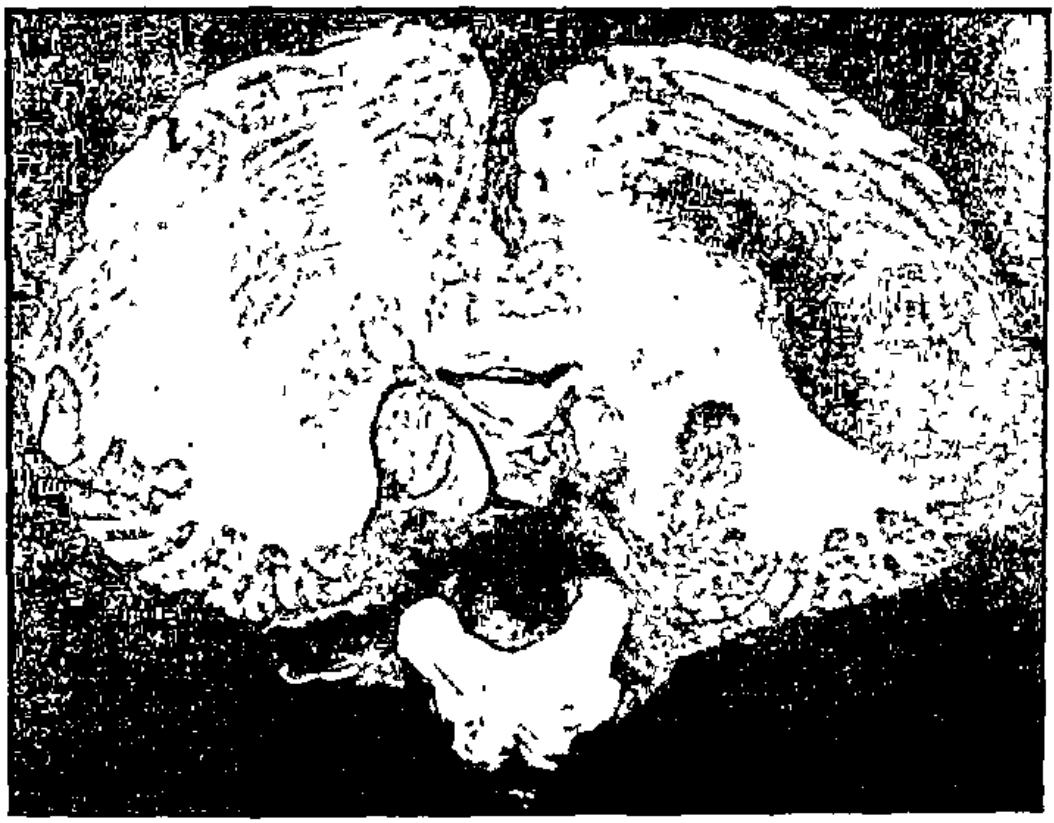


FIG. 45. *Case 36.* A chronic abscess just above the right foramen of Luschka is associated with occlusion of the latter, and ballooning of the left foramen. The dark area in right lobe is operation-haemorrhage

It is unfortunate that a full necropsy was denied in this case. The cerebellar abscess was presumably of pyaemic origin, but the source of the infection remains unknown. Histologically there is evidence of progression from an old but small abscess, which was responsible for the infection of the meninges over the pons, to the formation of additional abscess-cavities at deeper levels. The latter doubtless were responsible for the terminal rapid deterioration in the physical condition of the patient. The case demonstrates that expansion of the ventricular system may follow chronic purulent basal meningitis without concomitant pyocephalus.

Post-Meningitic Hydrocephalus

In the preceding cases it has been shown that internal hydrocephalus, with or without pyocephalus, complicates chronic purulent basal meningitis. To these examples others could be added, but it is unnecessary to enlarge upon what is obvious and universally acceptable. It forms, however, an essential preliminary to the consideration of a common form of internal hydrocephalus which is greatly in need of clarification. This, perhaps the most frequent form of chronic hydrocephalus in young children, forms a group comprising 23 cases in the series upon which the present study is based. About 50 per cent. (11 cases) were in children of six years or under. In general these appeared normal at birth, though occasionally a history of prematurity was obtained and in certain instances labour had been difficult. At some later stage gradual expansion of the head was noted, progressing often to a spectacular size over a period of many months, or even years. Ventriculography in these cases reveals a uniform enlargement, mainly affecting the lateral and third ventricles. The cerebro-spinal fluid shows no gross abnormality and is sterile on culture.

At necropsy there may be little to see beyond this expansion. But careful examination reveals a milky opacity in parts of, or throughout, the arachnoid of the basal cisterns, especially over the cisterna magna and the foramina of Luschka, which are often greatly ballooned. These sub-tentorial areas may, however, be relatively little affected and the thickening may affect rather the collar-like cisterna ambiens at the tentorial opening, or the cisterns abutting on the floor of the third ventricle. Such thickenings of the arachnoid are accompanied, at the borders of the cistern, by fibrous adhesions matting the subjacent pia which is fused with the arachnoid. Thus the cavity of the cistern becomes walled off and forms a veritable cyst. If a solution of dye, such as methylene blue, is carefully introduced into such a space in the fixed specimen it is retained in the cavity and cannot be massaged into the surrounding leptomeningeal spaces. This behaviour is in contrast with the ready diffusion that may be observed in the corresponding treatment of control specimens. This obstructive mechanism has been clearly demonstrated by Dandy (1921 *a*) and is regarded by him as a post-meningitic phenomenon. It has since been corroborated by Lindau (1928) and others, who again have attributed the condition to a preceding meningitis of infective or traumatic character. But the acceptance of this explanation rests upon the proof of such an antecedent meningitis, and unfortunately this is not forthcoming in the majority of cases. In the present group of 23 cases a history of infective meningitis is given in four cases, with bacteriological proof in two. Starting with these as a base upon which to build, it is proposed to examine the applicability of the theory to the group as a whole. A selection of cases will be described with this end in view.

Case 37: S.S., female aged 4 years (R.I. 5105/1939). This infant had been in good health until the age of 18 months when she had pneumonia complicated by meningitis. She was then in another hospital for 6 months, and a letter from the Medical Superintendent states that meningococci were obtained from the cerebro-spinal fluid. On leaving hospital she was free from symptoms, but from that time she never walked properly. About a month later she became listless and suffered from vomiting. The size of the head increased noticeably and she became fat. She was referred to the Nuffield Department of Surgery at the age of 4.
On examination: A fat child with a head measuring 55 cm. in circumference, and giving a cracked-pot note on percussion. There was bilateral secondary optic atrophy without papilloedema. *Coarse tremor of the upper limbs was accompanied by gross ataxia and slight* Rhombergism. *Lumbar puncture* yielded fluid under a pressure of 200 mm. containing 40 mg. per cent. of protein and 1 cell per c.mm. Cultures were sterile. *Ventriculography* revealed gross ventricular dilatation including the fourth ventricle. Subsequent cerebellar exploration proved negative save that the cisterna magna was unusually capacious. The foramen of

Magendie appeared normal. Following this operation there was no clinical improvement, so ventriculostomy was performed through the lamina terminalis 9 days later. The child died 5 days after this second operation.

Necropsy (R.I. P.M. 392/1939): No significant changes were found apart from the brain. The leptomeninges over the cerebral convexities appeared normal but were somewhat thickened and opaque in the cisternae interpeduncularis and ambiens, and over the anterior part of the vermis, the cerebellar tonsils and cisterna magna. There was ballooning of the arachnoid over the foramina of Luschka. All the cisterns appeared capacious except in the proximal parts of the Sylvian fissures, which appeared occluded by fibrosis. There was great dilatation of the ventricular system. The ependyma of the lateral ventricles was finely granular and thrown into irregular folds. The choroid plexuses were of normal appearance. *Microscopical examination*: There is slight fibrosis of the leptomeninges over the pons, accompanied by slight focal infiltration with groups of small lymphocytes and a few plasma cells. The fibrosis does not extend over the ventral surface of the cerebellum. In the Sylvian fissures fibrosis is very slight. The ependyma of the fourth and lateral ventricles is largely replaced by loose-textured neuroglia sparsely infiltrated with small lymphocytes and a few leucocytes. In places there is considerable subependymal gliosis In this layer the vessels are frequently cuffed with lymphocytes.

In this case the onset of the hydrocephalus was clearly related to an attack of meningococcal meningitis, for which there was bacteriological proof, two and a half years before death. But macroscopically and microscopically the amount of residual fibrosis was not impressive. Moreover some of the inflammatory cellular infiltration in the meninges and ependyma may have been caused by the operations carried out shortly before death.

In a second, somewhat similar case, in an infant of eight months, an attack proved bacteriologically to be meningococcal meningitis was followed after a few weeks, during which the inflammation appeared to have been resolved through intensive treatment with specific anti-serum, by the gradual onset of hydrocephalus and death after five months. By that time the head measured 57·5 cm. in circumference. Necropsy revealed gross internal hydrocephalus but there were no obvious changes in the leptomeninges. Microscopically however, there was slight fibrosis and sparse lymphocytic infiltration of the basal meninges. The main site of obstruction appeared to be in the cisterna ambiens.

Case 38: G H., female aged 3 years (R.I. 19190/1941): Admitted to the Nuffield Department of Surgery suffering from advanced hydrocephalus which dated from early infancy and was at first thought to be congenital There was a story of a febrile illness at the age of three weeks and, although the details were not sufficiently clear to establish its nature with certainty, it probably was a meningeal inflammation

On examination she was a fat, healthy-looking child, unable to sit or stand, with a head measuring 61·5 cm. in circumference. Her mental development appeared normal as judged by speech and behaviour There was low-grade papilloedema with normal visual acuity and full fields. Apart from slight hypertonia of the limbs and extensor plantar responses there were no further abnormalities. On *lumbar puncture* the fluid pressure was 240 mm. and contained 60 mg. per cent of protein and 2 cells. *Ventriculography* revealed gross dilatation of the whole ventricular system, including the fourth ventricle. *Ventriculostomy* through an opening in the lamina terminalis was performed, but the child died six days later.

Necropsy (R.I. P M 549/1941) There were no significant changes except in the brain. There was gelatinous grey thickening of the leptomeninges over the whole of the brain-stem, forming a pouch with well defined borders over each foramen of Luschka. In the basal and interpeduncular cisterns and the proximal parts of the Sylvian fissures a similar thickening was accompanied by brownish discoloration. The arachnoid roofing the cisterna magna was firmly adherent to the dura mater near the mid-line, its margins being thickened and slightly opaque. The cistern was greatly expanded, and the foramen of Magendie so large that the hind end of the aqueduct could be viewed through it (Fig. 46) The whole of the ventricular system was greatly expanded (Fig 47), the aqueduct measuring 0 7 by 0 5 cm in cross-section. *Microscopical examination*: The leptomeninges, especially the arachnoid membrane, over the brain-stem and cisterna magna are thickened by fibrosis and infiltrated with numerous desquamated arachnoid cells, many of which have ingested red corpuscles, while a few contain granules of iron pigment Free red cells and sparser leucocytes are also present. The arachnoid membrane over the cisterna magna is united to the dura by fibrous tissue, and here the arachnoid cells have proliferated to form sheets over the collagenous tissue. The fibrosis

does not extend however over the lateral lobes of the cerebellum, though phagocytic activity of the arachnoid cells is evident and is accompanied by a sparse infiltration with neutrophil leucocytes. There are numerous ependymal granulations in the lining of the fourth ventricle. The choroid plexus of the lateral ventricle is embedded in a richly vascularized layer of neuroglial and collagenous tissue infiltrated with a few lymphocytes and small groups of macrophages, many of which contain iron pigment.

FIG. 46: *Case 38* Section through fourth ventricle to show dilated foramen of Magendie

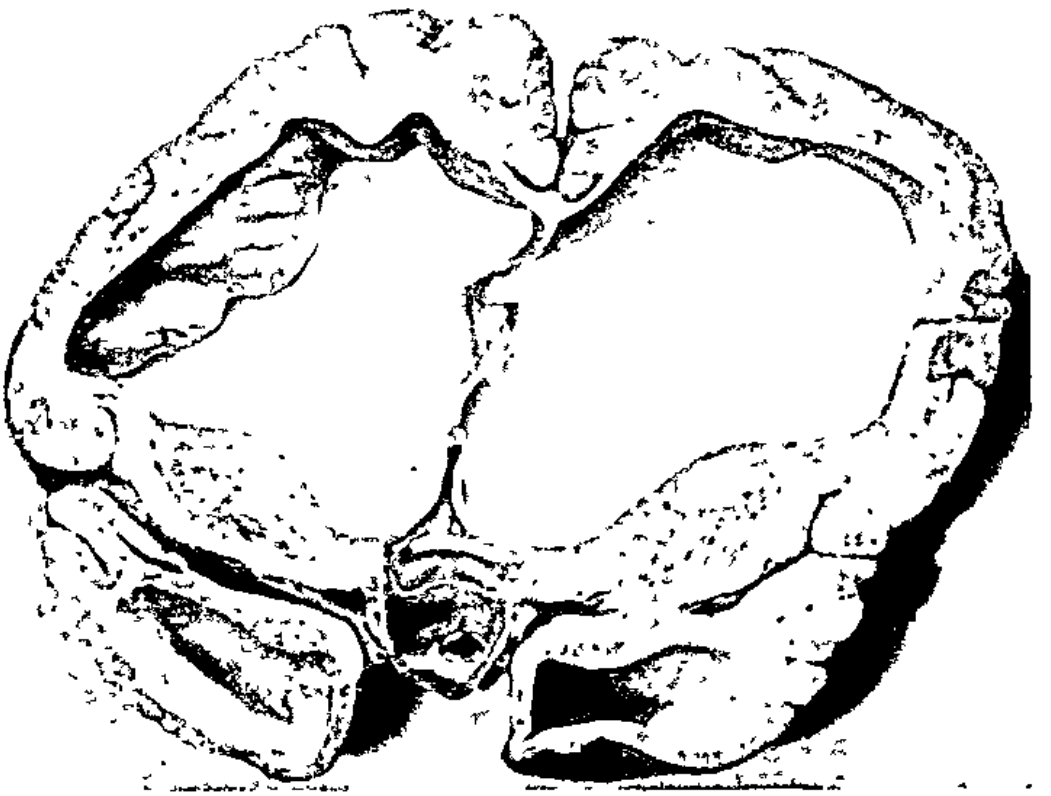


FIG. 47: *Case 38:* Ventricular dilatation following meningitis

Hydrocephalus was clearly due to a chronic meningitis of unknown ætiology. But the febrile illness at the age of three weeks may well have been associated with a low-grade meningitis. It is suggestive that expansion of the skull from this time was observed. There are insufficient grounds for attributing it to birth-trauma: the small amounts of iron-pigment present in the meninges and choroid plexus were accompanied, in other cells, by phagocytosed red corpuscles and should collectively be regarded as the result of the recent operations.

Certain macroscopic features in the lateral ventricles in this case, not germane to the immediate issue, have been described elsewhere (Pennybacker and Russell, 1943) and will be referred to in another context (p. 127).

In the following, somewhat similar, case the ætiology is completely obscure.

Case 39: J.E.K., female aged 17 months (R.I. 13515/1941): Admitted to the Nuffield Department of Surgery on account of progressive enlargement of the head, and inability to walk, crawl or sit up. She was the only child of her parents; pregnancy had been normal and delivery was by forceps after four hours of labour. No abnormality was observed at birth, but a week later, the mother noticed an asymmetrical bulging of the head on the left side which was attributed to birth-injury. Following this she had frequent tonic fits lasting for a few seconds during which all limbs were rigidly extended. Progressive enlargement of the head was noticed from the age of ten months onwards; this was not preceded by any recognized illness. Although she started to talk at eleven months she had not learnt to crawl or walk.

On examination the child appeared of poor mental development for her age. The head was considerably enlarged (54·5 cm. in circumference), and showed asymmetrical bulging of the left postero-parietal region and the right side of the forehead. Neurological abnormalities were confined to an increase of tone in all limbs, especially the lower, and increased tendon reflexes, with bilateral extensor plantar responses. There was ataxia of the upper limbs. It was considered on clinical grounds that the hydrocephalus was of the communicating type and due to birth-injury, but when 7 c.c. of indigo-carmine were injected into the left ventricle through the anterior fontanelle the dye did not reach the lumbar fluid until two hours later, when a trace was recovered. *Ventriculography* a week later showed gross internal hydrocephalus including the fourth ventricle. The child died six days after this, apparently from peripheral vascular failure.

Necropsy: (R.I. P.M. 113/1941): Relevant findings were confined to the head. There was marked expansion of the cerebral hemispheres, especially the left, and great ballooning of the floor of the third ventricle. The arachnoid membrane was dense and grey over the cisterna magna, which was small, and formed conspicuous pockets over both foramina of Luschka—that on the left measuring 2·5 by 2 by 1 cm. (Fig. 48). The leptomeninges were markedly thickened at the margins of these pockets, but this thickening did not extend over the adjacent cerebellum. A similar thickening was found over the anterior part of the pons with, in this area, a faint café-au-lait staining. In the cisterna magna the arachnoid was focally adherent to the dura mater, the inner surface of which showed a little orange pigmentation at the point of adhesion. The foramen of Magendie was occluded by fibrous tissue. The fourth ventricle was greatly enlarged, also the aqueduct which measured 0·5 cm. in diameter at the level of the posterior corpora quadrigemina. The cerebral tissue was reduced to a thickness of 0·8 cm. in places, and the septum pellucidum was greatly fenestrated. The ependyma was grey, glistening and corrugated. The choroid plexuses were small but appeared otherwise normal. No source of any haemorrhage was found nor any explanation of the slight asymmetry of the skull.

Microscopical examination: A mid-sagittal section through the hind part of the fourth ventricle shows occlusion of the foramen of Magendie by a septum of vascularized collagenous tissue with included strips of fibrillary neuroglia, one of which occupies the greater part of the length of the septum towards the cavity of the ventricle. The ventricular surface of the septum is coated in many places with a thick layer of leucocytes and lymphocytes. The remainder of the septum is infiltrated mainly with desquamated arachnoid cells. No iron pigment is present. There is fibrous thickening of the leptomeninges over the pons, accompanied by a moderate infiltration with leucocytes and lymphocytes. A few islands of fibrillary glia lie over the ventral surface. There is no iron or other pigment to account for the slight brown staining seen macroscopically. Much of the ependyma has been lost from the lining of the lateral ventricles. There is moderate subependymal gliosis and the vessels here are cuffed with lymphocytes, large mononuclear cells and a few leucocytes. A few early granulations are present in addition in the ependyma of the third ventricle. The stroma of the choroid plexus of the lateral ventricles is infiltrated with a good many leucocytes.

The hydrocephalus in this case was originally attributed to birth-trauma and haemorrhage. However, iron-pigment was found only in the area of adhesion

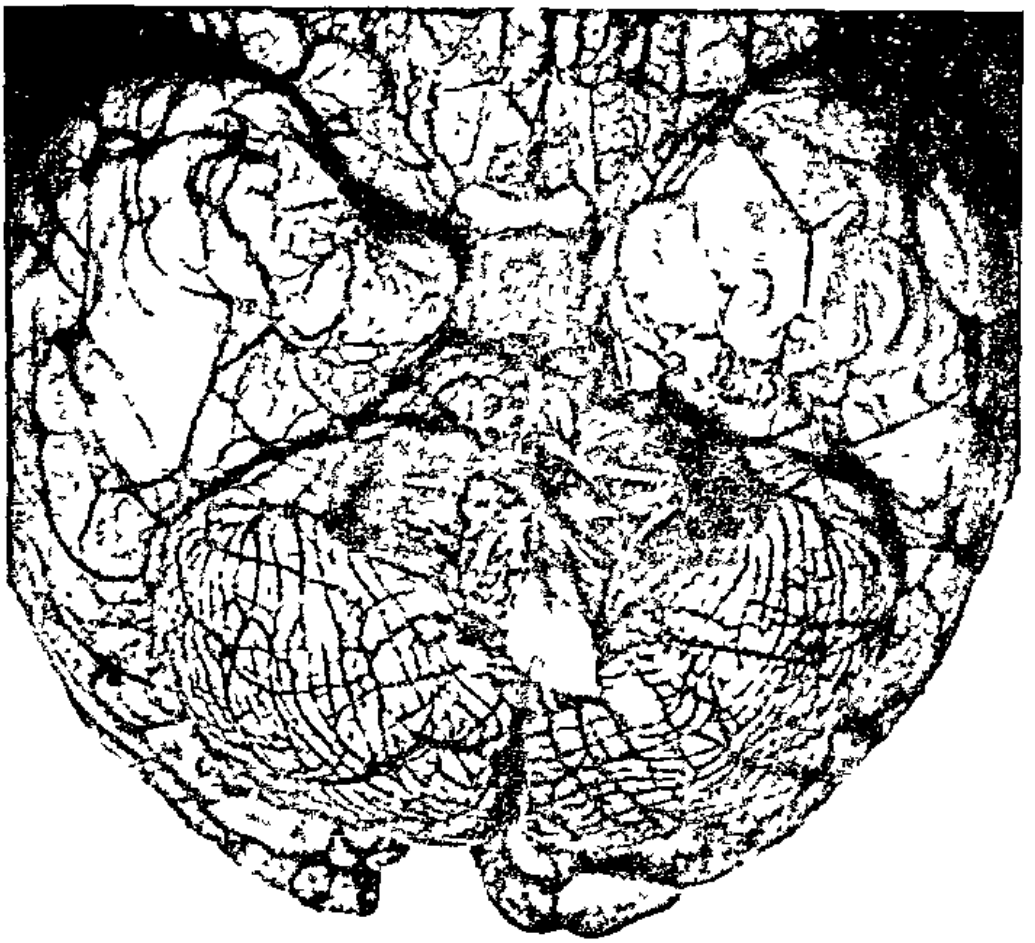


FIG. 48: *Case 39:* Cystic pocket over each foramen of Luschka These were filled with gelatin solution before being photographed

between dura and arachnoid over the cisterna magna. None was present in the leptomeninges, nor in the lining of the ventricles. This explanation is therefore unacceptable. But there is evidence of a low-grade ependymitis and meningitis which sealed off the foramen of Magendie and the margins of the foramina of Luschka. The presence of neuroglial tissue in the septum at the hind end of the fourth ventricle is not to be interpreted as a congenital malformation: the separation of such islands of tissue is frequently seen in infantile examples of chronic meningitis and is to be attributed to excessive proliferation of the *marginal glia which almost invariably accompanies such inflammations.* Greenfield and Stern (1932) observed similar islands in adults with syphilitic meningitis. The infiltration of certain areas with polymorphonuclear leucocytes is interpreted as an acute reaction to the intraventricular injection of indigo-carmine. The meningitis as a whole is therefore regarded as the sequel of a low-grade infection of unknown origin and duration.

The following case, in a younger infant, is somewhat similar.

Case 40: M.P., male aged 4¼ months. He was the only child of his parents and weighed 7 lb. at birth ; birth was normal. Except for a certain amount of nasal catarrh he progressed normally until five to six weeks before death when he had a cold in the head for one week. Following this his mother noticed enlargement of the head and "his eyes seemed to drop into his cheeks". He then became increasingly irritable and prone to vomit.

On examination One week before death he appeared pale and listless with a persistent cry and occasional tonic fits The head was enlarged, measuring 47 5 cm. in circumference: the sutures were separated and the anterior fontanelle bulged. No special investigations were carried out before death.

Necropsy: (R.I. P.M. 117/1944): A normally developed child. Apart from purulent bronchitis and slight focal broncho-pneumonia there were no changes except those in the head. The middle ears were dry. There was great ballooning of the arachnoid membrane over the cisterna magna and the interpeduncular fossa, and in the proximal ends of the Sylvian fissures. But the membrane appeared thin and translucent except at the margins of these spaces where it was opaque and tethered down to the pia. Elsewhere the leptomeninges appeared normal. The foramen of Magendie was so widely patent that the interior of the fourth ventricle could be viewed through it. There was great internal hydrocephalus ; the aqueduct measured 0·4 by 0·3 cm. in section through the posterior corpora quadrigemina. In the right lateral ventricle a papilloma measuring 3 by 1·5 cm was attached by a pedicle to the choroid plexus at the confluence of the occipital and temporal horns (Fig. 49).

Microscopic examination: The leptomeninges over the medulla oblongata, mid-brain and cerebellum show slight fibrous thickening of both the arachnoid membrane and pia, accompanied by moderate diffuse infiltration with large mononuclear cells, which occasionally show vacuolation of their cytoplasm, and small lymphocytes. There are occasional groups of polymorphonuclear leucocytes. No organisms were demonstrated by Gram's stain. The choroid plexus of the left lateral ventricle shows severe focal degeneration of the epithelium, the nuclei of the affected cells being pyknotic. The ependymal cells are missing from many areas in the portions of the lateral ventricles examined, but there is no evidence of ependymitis.

The tumour in the right lateral ventricle has the characteristic appearances of a papilloma of the choroid plexus.

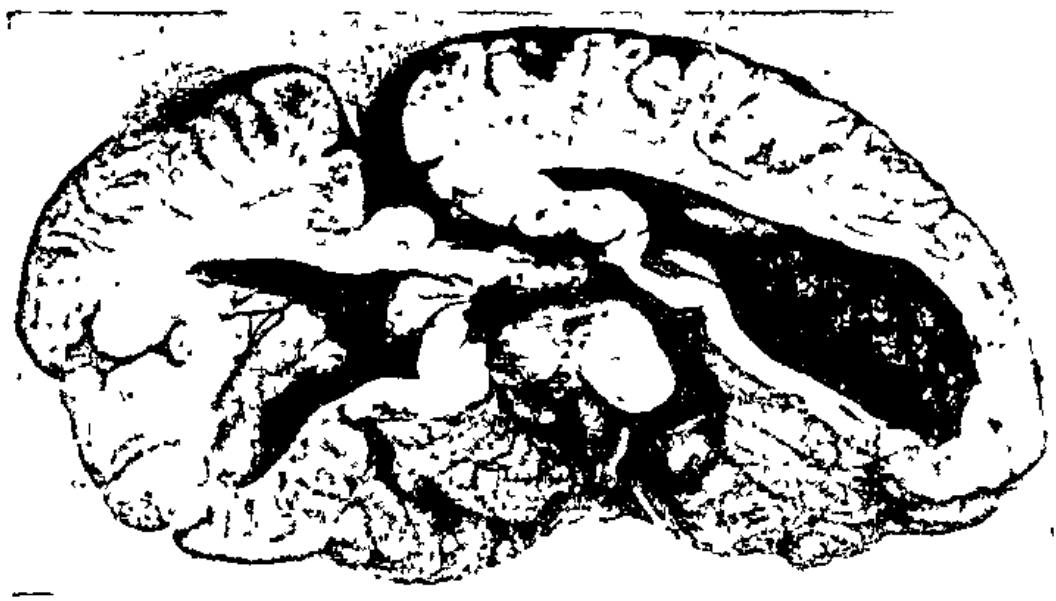


FIG. 49. *Case 40:* Ventricular dilatation following meningitis Papilloma of choroid plexus on right

Here, as in the preceding case (39), the naked-eye and histological appearances *are indicative of a low-grade meningitis with no clear evidence pointing either* to the time of onset of the disease or the character of the infective agent. The "cold in the head" which immediately preceded the observation of enlargement of the skull may have been significant but, in the absence of any recorded meningeal symptoms, this incident cannot be pressed in the service of explanation. The presence of a choroid plexus papilloma at this early age is remarkable ; it was presumably congenital. Reference has already been made to its association with hydrocephalus (p. 7): it is interpreted as a coincidental finding and of no ætiological significance.

Case 41: N B, female aged 30 years (Reg No. 40673/1934, Med.). Occupation: packer. She was admitted to the medical wards of the London Hospital on account of vomiting, headache, diplopia and photophobia of ten days' duration. She had had meningitis at the age of three, and scarlet fever at the age of twelve. She had suffered from occasional

headaches and vomiting throughout life. Fourteen days before admission she had fainted at work and was taken home. She complained then of giddiness, headache and double vision and was distressed by the light.

On examination she appeared healthy and well nourished. The pupils reacted poorly to light and accommodation. There was bilateral papilloedema, slight ptosis and coarse nystagmus on looking upwards and to the left. The other cranial nerves were normal. All limbs were hypotonic, the left arm being more affected than the right. There was slight intention tremor. All further neurological tests were negative. She collapsed and died a few hours after admission to hospital.

Necropsy: (P.M 182/1934): No significant changes were found except in the brain. This showed considerable flattening of the cerebral convexities and bulging of the floor of the third ventricle. Apart from conspicuous ballooning of the arachnoid membrane over the foramina of Luschka (Fig. 50), from which clear cerebro-spinal fluid gushed out during removal of the brain, there was no further macroscopic evidence of meningitis The foramen of Magendie appeared normal. There was great distension of the whole ventricular system including the fourth ventricle The ependyma everywhere was smooth and glistening, and the choroid plexuses appeared normal.

Microscopic examination: There is slight fibrosis without cellular infiltration of the pia over the ventral surface of the pons and medulla oblongata, and about the meningeal blood-vessels. In the interpeduncular fossa the meninges are sparsely infiltrated with small lymphocytes. The choroid plexuses in the foramina of Luschka are greatly flattened. In the floor of the fourth ventricle the ependyma is intact but is raised into small granulations in a few places. The aqueduct, which is dilated, is lined in places with normal ependyma, but elsewhere by glial tissue which has grown inwards centripetally, leaving tubules and small isolated groups of ependymal cells in a zone remote from the lumen. The ependyma is also missing from many parts of the lateral ventricles, but the lining is free from granulations. The choroid plexus of the right ventricle appears normal

FIG. 50: *Case 41:* Ballooning of arachnoid membrane over right foramen of Luschka. That on the left has collapsed

It is remarkable that the hydrocephalus, which must have been of long standing, should have proved so suddenly fatal. The pathological examination

provides no explanation of the terminal collapse of the patient. The case is one of several in the present series in which post-meningitic hydrocephalus clinically simulated a cerebellar tumour: a resemblance that has previously been pointed out (Horrax, 1924; Barrê, 1933; Worster-Drought and Knight, 1939). The gush of cerebro-spinal fluid from the pockets over the foramina of Luschka when the seventh and eighth nerves were divided in removing the brain indicated an obstruction at this point. In other respects the evidence of a preceding meningitis was scanty. In attributing the hydrocephalus to the attack of meningitis in early childhood, of which no further information was obtained, support is provided by the closely similar case reported by Baker (1934). In this a girl of 17, working in a factory and admitting no previous illness, complained for three weeks before death of headache, vomiting and pain between the shoulder blades. At necropsy internal hydrocephalus was associated with old adhesions at the base of the brain. It was later discovered that she had been admitted to Guy's Hospital with meningitis at the age of eighteen months, and that meningococci had then been found in the cerebro-spinal fluid. At the end of this illness she had been discharged as cured with no apparent complications. There can be little doubt therefore of the curious latency of this post-meningitic form of hydrocephalus. If this is admitted then it might well be supposed that cases with less advanced degrees of hydrocephalus might occasionally be encountered by chance at necropsy where death has been due to some unrelated condition. This in fact is true: in the course of compiling the present series examples have been investigated in the postmortem room in which a moderate dilatation of the ventricles has been associated with a milky opacity of the arachnoid at the base of the brain over some or all of the fourth ventricle foramina. In none of these cases was a history of antecedent meningitis recorded, but no specific enquiry had been made during life. Outstanding in this group on account of the surprising degree of hydrocephalus attained without symptoms is the following case which must be regarded as exceptional.

Case 42 E K., female aged 49 (Reg. No 50394/1943). The patient was a married woman with one child who was admitted to the gynaecological wards of the London Hospital suffering from abdominal pain of two months' duration. There was a history of influenza and pleurisy at the age of five years but, apart from this, she appeared to have led a healthy life up to the time of the present illness

On examination she was pale and well nourished, lethargic and drowsy, with a tendency to become emotional. No note of the nervous system was entered apart from an examination of the pupillary reflexes, which were normal. A pelvic tumour was found which on laparotomy proved to be a cystic carcinoma of the right ovary. A portion was removed for biopsy. The patient died two months later.

Necropsy (P M 162/1943). *Oedema of lungs. Small pulmonary emboli. Ascending pyelonephritis. Cystic carcinoma of right ovary.*

The brain (Fig. 51) showed dense grey fibrosis of the leptomeninges at the base above the level of the tentorium, and surrounding the mid-brain. Within the fibrous tissue were cystic spaces, measuring up to 3 by 2 cm., which occupied the proximal ends of the Sylvian fissures causing considerable deformity of the temporal poles, and also formed pockets within the cisterna ambiens on either side of the pineal body. The inner surfaces of these cysts appeared smooth and completely walled off from the surrounding meningeal spaces. Slight milky-white fibrous thickening affected the leptomeninges over the hind-brain and the central third of both cerebral convexities. There was excessive bulging of the floor of the third ventricle (Fig. 51). This was but one feature of the ventricular enlargement, shown in Fig. 52. The aqueduct was greatly dilated, measuring 0·5 by 0·35 cm. just anterior to the fourth ventricle, but the latter was not appreciably affected. The foramen of Magendie was patent; the foramina of Luschka were probably sealed as there was slight ballooning of the arachnoid over both of them. There was fenestration of the septum pellucidum and slight atrophy of the choroid plexuses. The ependyma was everywhere smooth, but was marked in many areas with shallow pits and serpiginous grooves.

Microscopic examination: The histological appearances confirm the above features. The thickened meninges are sparsely infiltrated with scanty mononuclear cells and small lymphocytes. The choroid plexus of the fourth ventricle appears normal. The lateral ventricle is lined in places with ependyma and elsewhere by the greatly thickened subependymal glia. The blood-vessels in this layer frequently show marked collagenous thickening of their walls.

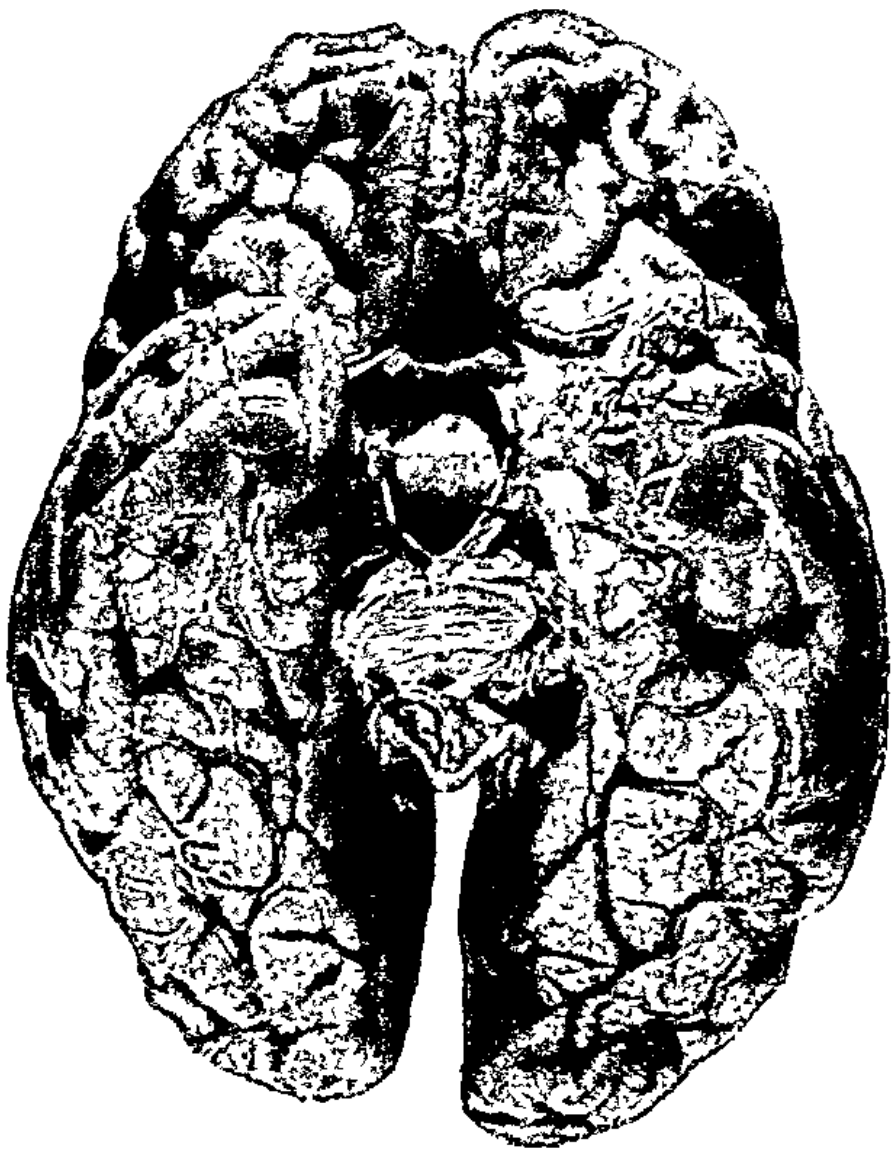


FIG. 51: *Case 42:* Base of cerebrum. The meninges have been dissected to show bulging of floor of third ventricle. The sheet of fibrous arachnoid membrane has been left intact over the proximal part of the left Sylvian fissure

Possibly a detailed neurological examination of this patient would have revealed some objective signs and symptoms. The lethargy and emotional instability recorded in her notes may be linked up with the exceptional distension of the floor of the third ventricle and consequent hypothalamic disturbance. Even so it is surprising that so great a degree of hydrocephalus

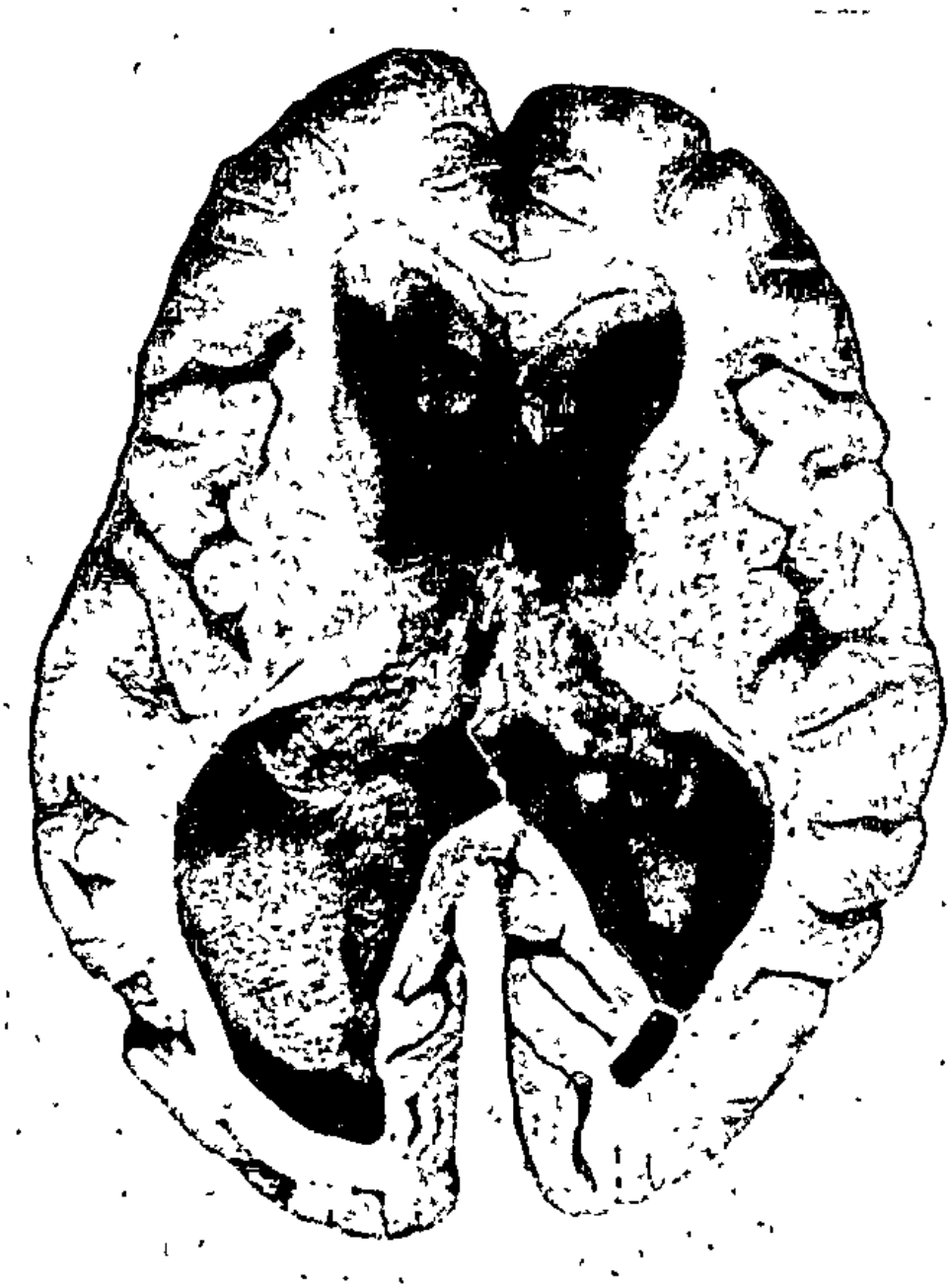


FIG 52: *Case 42:* Internal hydrocephalus, unsuspected clinically, in a woman of 49

should have created so little clinical effect. The meningitis was of great chronicity and may have dated back to the attack of influenza and pleurisy in early childhood, but this must rank as pure speculation.

DISCUSSION

The clinical and pathological aspects of post-meningitic hydrocephalus have been considered at some length because it is perhaps the most obscure and difficult to explain of all types of hydrocephalus. As Dandy (1921a) has already recognized, it is the variety that goes by the name of "idiopathic"; but the term "cystic arachnoiditis", which is purely descriptive and non-committal, would be a better alternative were it not that it has been loosely

and indiscriminately used by ophthalmic and neurosurgeons. The cases that have been described are a fair sample of the total number observed, and they show that in some instances there is proof of an initial infective meningitis. Such cases, however, form a minority. The meningococcus seems, both from the present series and from already published reports, to be more often responsible than any other organism (see Dott and Levin, 1936). Hinds Howell (1936) relates "cystic arachnoiditis" to an antecedent attack of meningococcal meningitis, particularly in those cases in which the arachnoiditis is localized in the posterior fossa.

But in many cases there is no history of such an infection, or the hydrocephalus may have been ushered in by an infection of the respiratory or intestinal tract. In such cases the meninges may have been involved, and this possibility is undoubtedly greater in the infections of infancy than in later life. The liability of infants to infection with coliform bacilli has already been mentioned (p. 69). It has been shown (Cooke and Bell, 1922) that the normal agglutinins for *Bact. coli* are absent in the newborn. The extra vulnerability of the premature infant was clearly brought out in Craig's series (1936) in which the majority of cases of neo-natal meningitis were in premature babies.

Fraser and Dott (1922-23) consider that the frequency of infective meningitis in early life is probably underestimated. Such infections, in their opinion, are not necessarily fatal; some are so slight that they may be masked clinically by the general symptoms. The generalized character of neo-natal infections has received recent comment from Parsons (1944), and from Spence (1941) who points out that, whereas in older children and adults the recognition and classification of infective diseases on an ætiological basis is relatively easy, "in infants not only may the causative organism be difficult to recover, but the pattern of the illness following any known infection is so variable as to give little help in diagnosis. A bacillus dysenteriæ Flexner infection may cause generalized toxaemia in one infant, meningitis in another and dysentery in another; two infants may be similarly infected and both may die, yet in one the illness may have been febrile and in the other afebrile . . . An organism such as the *B. coli* which is relatively innocuous to older children may cause a rapidly fatal illness in a newborn infant". In their impressive series of 705 cases of meningitis in infants and children Fothergill and Sweet (1933) note a high incidence of infection during the first two and a half years of life. The meningococcal (160 cases) and influenzal (78 cases) examples mostly occurred in the second half of the first year; haemolytic streptococcal and pneumococcal infections (69 cases in each group) however showed their highest incidence in the first six months of life. Meningitis in the newborn was usually due to one or other of these last-mentioned infections or to *Bact. coli* (9 cases). In addition to neo-natal infection the possibilities of intra-uterine foetal infection in association with prolonged labour and maternal infection require further investigation in view of the work by Douglas and Stander (1943) who obtained a positive blood-culture from the heart in such cases in a large series of still-births. In the majority of a larger control series, in which death was clearly due to some other factor such as intracranial haemorrhage, the blood-cultures were negative. The question is obviously of great importance in connection with certain cases of hydrocephalus that appear to develop shortly after birth, and are not directly attributable to birth-trauma. Given that such a blood-infection does in fact occur during labour, the liability for organisms to pass into the leptomeninges deserves special consideration

when it is recalled that, experimentally, a venous stasis of two minutes' duration induced by compression of the jugular vein is sufficient for this to occur in the adult animal (Weed *et al.*, 1920). Should the infant sustain a non-fatal intracranial haemorrhage during labour this may prove an additional factor favouring infection of the meninges. The following case is of exceptional interest since it appears to be an instance of this kind.

Case 43: J.S., male aged 5 weeks (Reg. No. 12031/1932). The infant, the first child of its parents, was born by forceps delivery after a labour lasting two days. There was paralysis of the left side of the face. The head, which had been of normal size, began to enlarge at the end of two weeks. Pyrexia and convulsions began at the eighth day after birth and continued from that time onwards.

On examination, four days before death, the head was 43 cm. in circumference, with separation of the sutures and bulging fontanelles. The head and eyes tended to be fixed towards the right. There were occasional nystagmoid movements to the right, occasionally a convergent squint of the left eye. There was gross weakness of the left side of the face, but no paralysis of the limbs.

Puncture of the left ventricle yielded yellow turbid fluid from which *Bact. coli* was cultured.

Necropsy. (P.M 254/1932): An organizing haematoma containing purulent foci occupied the subdural space beneath the tentorium, which was intact. Similar haematomata were present in the leptomeninges over both temporal poles and were bound down to the dura by delicate rusty adhesions. Inspissated pus filled the basal cisterns but faded away over the cerebral convexities. A rusty red membrane occluded the foramen of Magendie. The ventricular system was dilated and contained thick shreddy pus which obscured the choroid plexuses. There was diffuse orange pigmentation of the pia-arachnoid of the spinal cord. The source of the haemorrhage was not found.

Microscopical examination. In addition to confirming the macroscopic findings, the examination disclosed an advanced ependymitis in the lateral and fourth ventricles, the epithelium being replaced by young granulation tissue infiltrated mainly by large mononuclear cells, while the subependymal vessels are cuffed with small and large lymphocytes and plasma cells. Similar granulation tissue covers the choroid plexuses. The meningitis over the brain-stem is in a chronic purulent stage characterized by fibrosis and the formation of young granulation tissue, while the cellular infiltration about pockets of old pus in the arachnoid spaces is mainly composed of large mononuclear phagocytes and lymphocytes.

In this case, therefore, there was a clear history of birth-trauma, confirmed at necropsy. This was associated with a purulent meningitis and pyocephalus which, histologically, had reached a stage of sufficient chronicity to indicate its acquisition at, or shortly after, birth. The organism was of coliform type. The formation of small abscesses in the haematomata suggests that the latter provided good soil for growth. But the source of this infantile infection, and its path to the blood-stream and thus to the meninges remain obscure. However Craig (1936) found that meningitis in these neo-natal cases was often only recognized after death. During life pyrexia might be absent or appear only at a late stage of the attack; the pressure of the spinal fluid was often normal or even low. He considered that incoordination of the eye-movements and nystagmus were the most helpful clinical signs, especially if these were associated with restless movements of the head.

This problem of neo-natal meningitis has been considered at some length because in the cryptic character of the disease may well lie the explanation of a type of hydrocephalus that has always proved difficult to elucidate.

Granulomatous Inflammations

The principal granulomatous inflammations occurring in this country, tuberculosis and syphilis, have been relegated to the tail of this section because they do not bulk largely at the present time in any representative series of hydrocephalics.

Variable, usually slight, degrees of ventricular dilatation accompany most cases of tuberculous meningitis (Fig. 85, p. 124). But the disturbance

occasioned by this is overshadowed by the meningitis itself which usually proves fatal before sealing of the cerebro-spinal pathways has become complete. This is the "acute hydrocephalus" of the past century and a half. It must be with extreme rarity that such infections subside to reach a quiescent, fibrotic stage with a more advanced hydrocephalus. But Barnes (1939) has had experience of such a case. None has been recognized in the course of the present study.

A tuberculoma may, like any tumour, cause hydrocephalus should it be suitably placed within the brain. Parker and Kernohan (1933) have described such an example in the mid-brain occluding the aqueduct.

The role ascribed to syphilis in the causation of hydrocephalus has varied widely in the past according to the epoch at which the study was made, and the colouring lent to the interpretation by the writer's outlook. In retrospect it seems as though the criteria used for the diagnosis of syphilis have often been of the flimsiest and this, of course, is particularly true of the pre-Wassermann days. Nevertheless syphilis has for many years been given pride of place in textbook accounts of hydrocephalus. Amongst present-day observers there is considerable divergence of opinion. Thus Fraser and Dott (1922-23) say "we have been surprised to find what a relatively large proportion of hydrocephalics are victims of congenital syphilis and show a positive Wassermann reaction". They associate the infection with basal plastic and adhesive meningitis and with "atresia" (presumably of the aqueduct). They believe that a considerable proportion of such atresias are "specific" in origin and can be arrested by anti-syphilitic measures. In stressing syphilis as a cause of hydrocephalus they concur with many earlier writers on the subject such as d'Astros (1898), and certain recent authorities such as Jeans and Cooke (1930), who found hydrocephalus in some degree in nearly one-third of the children in their clinic presenting clinical evidence of neurosyphilis. The cerebro-spinal fluid in these cases suggested a mild degree of meningo-vascular syphilis. Treatment proved effective and no necropsy studies were available. But their statement that "one of the most marked had a head circumference of 46 cm. at five and one-half months" shows that the degrees encountered must in general have been slight, and goes a long way towards explaining the divergent views of clinicians and pathologists in this matter. Yet de Lange (1929) and Marburg (1940) considered that syphilis, though accounting for some cases of hydrocephalus, is not as frequent as many have supposed.

Reasons have already been given (p. 16) why atresia, or forking, of the aqueduct should be interpreted as a malformation and not an inflammation. Again no evidence was found in favour of a syphilitic basis for the condition known as gliosis of the aqueduct (p. 50), though this may indeed be an inflammatory condition. Amongst the types of meningitis discussed above it might have been anticipated that syphilis would have been found, especially in the post-meningitic group of hydrocephalics of obscure ætiology. No evidence of the kind, however, has been disclosed in a single instance. With one doubtful exception no example of proved syphilitic infection has been identified in any hydrocephalic subject upon whom necropsy has been performed in the Bernhard Baron Institute at the London Hospital since 1907. Allowing for the possibility that a few may have escaped detection, the conclusion seems inescapable that syphilis is, at the present time, a very rare cause of advanced hydrocephalus in this country.

Occasional examples, however, undoubtedly occur. Such a case was

encountered in a woman aged 42, who was admitted to the Nuffield Department of Surgery in 1943. Ventriculography revealed marked internal hydrocephalus and a cerebellar exploration was performed on the expectation, from the symptomatology, of finding a tumour in this situation. But an adhesive meningitis was disclosed, with grey granulomatous tissue infiltrating the tonsils. Histological examination of a fragment of this tissue revealed a granulomatous inflammation of the meninges and subjacent cerebellar tissue, with the formation of minute gummata in the tonsil. The arachnoid membrane from the cisterna magna showed great fibrous thickening with focal lymphocytic infiltration. The Wassermann reaction of the spinal fluid was then found to be strongly positive. The patient improved on a post-operative course of anti-syphilitic treatment, and was eventually discharged.

A series of seven such cases in adults is described by Greenfield and Stern (1932). They were characterized by a gummatous type of meningitis over the brain-stem causing obstruction to the fourth ventricle foramina, and by a granulomatous ependymitis of this ventricle.

In one case in the present series, in an adult, the histological picture is strongly suggestive of syphilis, but there is no confirmatory clinical evidence.

Case 44. G.B., male aged 43 (Reg. No. 10468/1933). The patient was admitted to the London Hospital for attacks of giddiness and vomiting during the preceding six months. He denied any previous illness except influenza. The attacks were of sudden onset without premonitory symptoms. He fell to the ground unless supported, but did not lose consciousness. After the attack, which lasted about fifteen minutes, he vomited. He would have up to two or three attacks daily. Latterly he had also complained of headaches, weakness of the legs, vertigo and increasing deafness.

On examination there was suboccipital tenderness, bilateral papilloedema and lateral nystagmus. On the right side the corneal reflex was absent, there was slight weakness of the lower part of the face, moderate deafness and complete absence of vestibular response and slight weakness of the palate. The left abdominal reflexes were greatly diminished. He was unsteady in walking and standing, with a tendency to fall to the right. There was slight hypotonia of the right arm and leg, and slight postural loss in the right thumb and right big toe.

The Wassermann reaction was negative in both blood and cerebro-spinal fluid. The latter contained 220 mg. per cent. of protein, and 10 lymphocytes per c.mm.

A cerebellar exploration for a suspected right cerebello-pontine tumour proved negative and the patient died under the anæsthetic from blockage of the intratracheal tube.

Necropsy (P.M. 96/1933): No significant changes were found except in the central nervous system. The heart weighed 12½ oz. and there was slight general atheroma. Fibrous pleural adhesions were present over the left lung. The liver and kidneys were congested.

Brain: There was great milky-white opacity of the basal lepto-meninges, obscuring the nerve-roots and main cerebral arteries (Fig. 53). Delicate fibrous adhesions united the arachnoid and dura about the sella turcica and over the brain-stem. The fibrosis of the meninges extended forwards to the olfactory bulbs and into the great longitudinal and Sylvian fissures, but became faint over the cerebral convexities. The arachnoid roofing the cisterna magna was opaque and white. There was great dilatation of the ventricles, including the fourth, but not of the aqueduct which was normal in size. The ependyma was smooth and glistening for the most part, but showed minute granulations and wrinkles in places. The choroid plexuses were atrophied and buried in bluish-grey fibrous tissue.

Over the spinal cord the arachnoid membrane was thickened and opaque, and matted to the dura by delicate fibrous adhesions which were condensed into a thick transverse ridge over the posterior surface of the eighth thoracic segment. The sacral roots were embedded in a mass of dense hyaline fibrous tissue which completely filled the lowest 3 cm. of the theca. The substance of the spinal cord appeared normal.

Microscopical examination: The fibrous leptomeninges over the brain-stem are infiltrated with a moderate number of small lymphocytes, a few plasma cells and a good many large mononuclear cells. The infiltration extends into the cranial nerve-roots along the blood-vessels, and for short distances into the brain substance along the perforating vessels. There is marked intimal hypertrophy of the meningeal arteries, and severe endarteritis obliterans in one of these at the lateral border of the medulla oblongata. The lining of the fourth ventricle is denuded of ependymal cells and is composed of oedematous neuroglia infiltrated with a few plasma cells and small lymphocytes. The choroid plexus of the left ventricle is atrophied and overlaid with collagenous tissue infiltrated with small lymphocytes. Numerous granulations are present in the adjacent ependyma.

In the spinal cord there is a similar meningitis with chronic pachymeningitis at the level of the eighth thoracic segment, the dura here being diffusely but sparsely infiltrated with small lymphocytes and fibroblasts. Beneath this, one of the dorsal veins of the cord has undergone thrombosis and recanalization. Elsewhere the meningeal arteries over the cord show intimal hypertrophy. There is early endophlebitis of a pial vein over a dorsal column in the fifth thoracic segment. *Apart from slight marginal demyelination the cord appears normal.* The fibrosis at the tip of the sacral theca is relatively acellular, the greatest cell aggregates being about the blood-vessels in the nerve-roots. Near the periphery of the theca a few areas of lamellar bone, containing small medullary spaces, have been laid down.

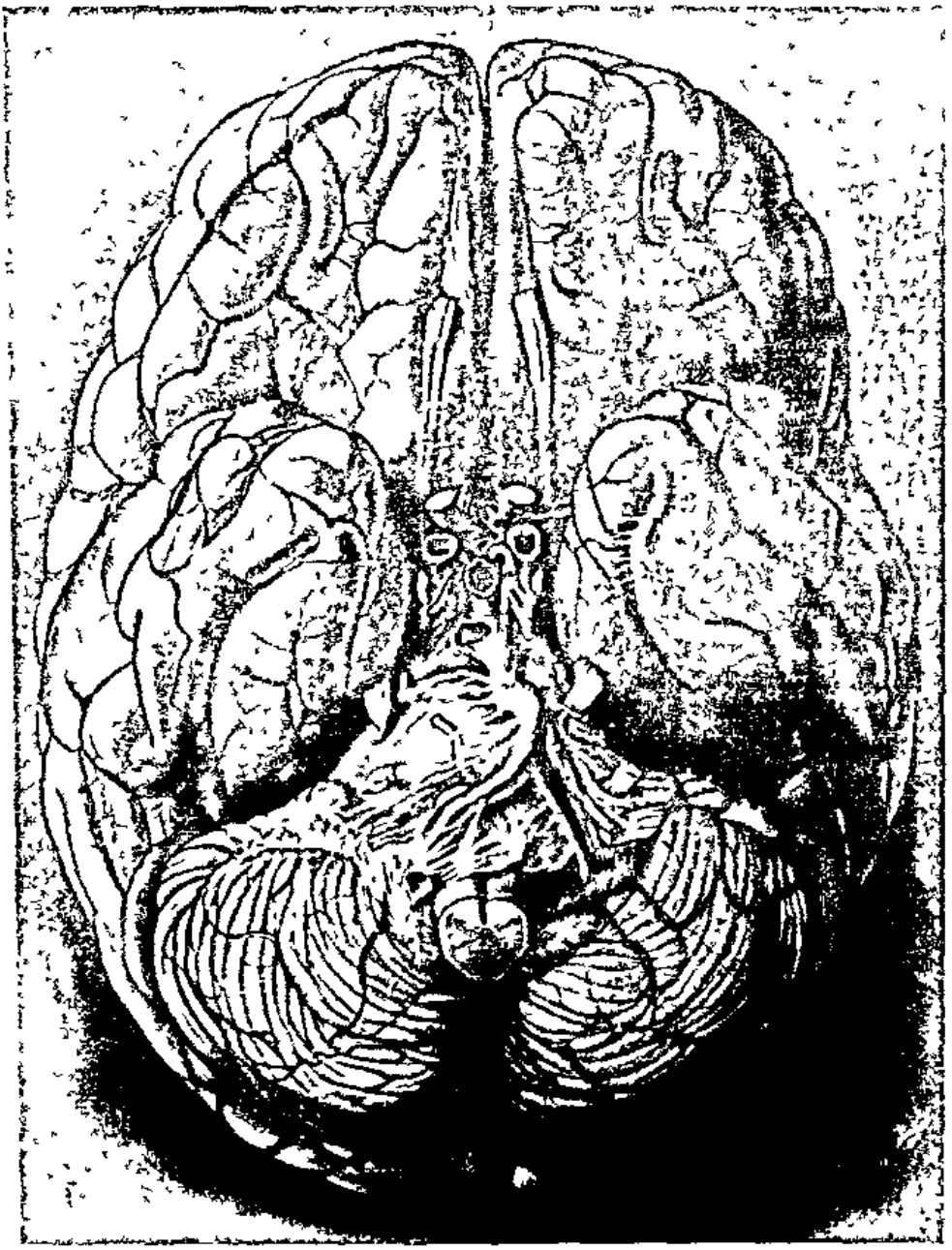


FIG. 53: *Case 44:* Drawing of base of brain showing the distribution and great density of the arachnoid fibrosis

Despite the negative serological tests in this case the histological appearances of the brain and spinal cord indicate a chronic progressive granulomatous inflammation, and are more suggestive of syphilis than of any other known infection. It is noteworthy that in Case I of Greenfield and Stern (1932) the Wassermann reaction was negative, and in Case 4 it was doubtful. The pathology of this present case is in many respects similar to that described by Greenfield and Stern.

CHAPTER V

DURAL SINUS THROMBOSIS AND THROMBO-PHLEBITIS

It has been pointed out (p. 9) that retardation of absorption of the cerebro-spinal fluid into the venous blood through the arachnoid villi is at least a theoretical cause of hydrocephalus. If the villi or the vessels, into which the cerebro-spinal fluid is passed, should become blocked, then it would be reasonable to expect that the fluid would be dammed back first into the leptomeningeal spaces and later into the ventricular system, with an accompanying increase in intracranial pressure and dilatation of the ventricles. This in fact is the mechanism that has been postulated in "otitic hydrocephalus" (Symonds, 1931 ; 1937), a clinical syndrome in which raised intracranial pressure and papilloedema may be associated with sinus thrombosis, but unaccompanied by infection of the leptomeninges or by cerebral abscess. The name is rather misleading in that it suggests an essentially inflammatory process originating in the middle ear ; but the clinical syndrome, so far as histological evidence goes, is associated with a sinus thrombosis which is histologically aseptic and may be initiated in the superior longitudinal sinus quite independently of a pre-existing otitis media. The existence of the syndrome is undisputed, but the question whether internal hydrocephalus is a sequel to it is highly controversial. Thus Gardner (1939) states that the ventricles in these cases are normal or even reduced in size. The fact that lateral sinus thrombosis is commoner than otitic hydrocephalus suggests that this factor alone is generally insufficient. Possibly an extension of the thrombosis into the superior longitudinal sinus is an essential complication. Since the right lateral sinus usually forms the anatomical continuation of the superior longitudinal sinus, while the left unites with the straight sinus it follows that, if thrombosis of the superior longitudinal sinus is a necessary factor, then otitic hydrocephalus should complicate a right otitis media rather than a left. According to Symonds the clinical figures support this view but are as yet too scanty to be conclusive. There seems to be no doubt, from reported cases, that a retrograde sinus thrombosis can in fact ascend from the lateral to the superior longitudinal sinus ; moreover it seems to be established that hydrocephalus may follow thrombosis of the superior longitudinal sinus alone. Such a case was investigated clinically by Ellis (1937) in an infant of 5 months who had developed multiple thromboses following jaundice at the age of 5 weeks. The fontanelle at that time was tense and there was slight separation of the sutures, the circumference of the head being 41·3 cm. The cerebro-spinal fluid was under increased pressure and contained blood, but was sterile on culture. The fluid became clear at the end of two weeks and was thereafter normal. Gradual enlargement of the head was subsequently observed and, at the age of 3 months, the circumference was 43·7 cm. Great ventricular dilatation was then demonstrated by ventriculography, and the Queckenstedt test showed no rise in cerebro-spinal fluid pressure when either right or left jugular vein was compressed. At the age of 5 months blockage of the superior longitudinal sinus was demonstrated radiographically following the injection of 4 c.c. of "Perabrodil" into the sinus: the block lay 2½ inches posterior to the anterior fontanelle. Six months after this the child was still living and had undergone no obvious change (personal communication).

In 1937, Bailey and Hass reported three similar cases in young subjects all of whom came to necropsy. In two, both infants, the thrombosis was confined to the superior longitudinal sinus and followed an attack of gastro-enteritis.

Personal experience of progressive sinus thrombosis has been scanty but, from the material available for study, it is tentatively suggested that sinus thrombosis may be followed by a limited degree of internal hydrocephalus after the lapse of a certain length of time, perhaps a few weeks, and that the size of the ventricles may revert to normal, or almost normal, with canalization of the thrombus. The admittedly fragmentary evidence will be presented.

First it is certain that sinus thrombosis is not immediately productive of any dilatation of the ventricles. Marantic thrombosis of the superior longitudinal sinus is frequently seen in young infants dying from a wasting disease. In these the thrombosis is obviously recent ; there is no evidence of organization. In some instances there is little gross change in the macroscopic appearances of the brain. In others there are profound circulatory disturbances, with considerable areas of haemorrhagic infarction in the cerebral hemispheres. The brain is swollen and the ventricles small. In such cases there may be bulging of the anterior fontanelle shortly before death. A typical example is given.

Case 45: G S, a male infant aged 5 weeks (Reg No. 30284/1939) He was admitted one week before death suffering from catarrhal gastro-enteritis of three days' duration.
On examination he was a small, wizened infant with slight depression of the anterior fontanelle and loss of elasticity of the skin. The ears appeared normal In spite of treatment vomiting continued and his condition steadily deteriorated Lumbar puncture, five days before death, yielded normal cerebro-spinal fluid. Increased tension of the anterior fontanelle was observed on the day before death.
At *necropsy* (P M. 68/1939) antemortem thrombus was lightly adherent to the intima throughout the superior longitudinal sinus, the medial part of the right lateral sinus and the greater part of the left lateral sinus There was no excess of fluid in the subdural space. The cerebral hemispheres were considerably flattened and the superficial cerebral veins over the frontal and parietal lobes were distended with thrombus. An area, 3 cm in diameter, of haemorrhagic infarction occupied the upper right Rolandic area. There was a little blood-stained fluid in the basal cisterns. The ventricles were of normal size.

In the three cases now to be described thrombosis of the dural sinuses and cerebral veins of longer duration was associated with ventricular dilatation.

Case 46. J.M., a female infant aged 6 months (Reg. No. 41715/1932): Birth had been normal (weight 6 lb. 5 oz.). About six weeks before death there had been discharge from the right ear. *This ceased three weeks before death and, at that time, she developed a feverish cold* followed by swelling of the frontal region and a squint She cried continuously, and there was slight cough and vomiting. On admission to hospital, ten days before death, the head was enlarged (49 cm. in circumference) with bulging of the fontanelle, which was enlarged The head and eyes were deviated to the left. The discs were normal ; ocular movements *were full and the pupils rather dilated No further neurological abnormalities were found* beyond loss of power in the right arm and left leg Three days later, *i e.* one week before death, puncture of the right ventricle yielded clear fluid under pressure in which the Wassermann reaction was negative and there was no excess of cells or of protein
Necropsy (P M. 496/1932): *Internal hydrocephalus Thrombosis of dural sinuses and of veins of Galen.* Apart from parenchymatous degeneration of the myocardium, liver and kidneys there was no macroscopic abnormality in the rest of the body. No evidence of tuberculosis was found. The body was well developed and nourished
Examination of head and brain The cranial bones were thin and translucent. Pus was present in the right middle ear ; the left was normal. Lightly adherent antemortem thrombus filled the superior longitudinal sinus, straight sinus, great vein of Galen and the adjacent medial part of the left lateral sinus. Similar thrombus distended numerous superficial veins, especially in the parieto-occipital regions. There was no macroscopic evidence of meningitis. *A suspension of India ink (7 5 c c.) had been injected into the right lateral ventricle immediately* before death, and particles of this were profuse throughout the basal cisterns, extending anteriorly to the optic chiasma, and less numerous over the dorsal aspect of the cerebellum and olfactory tracts. None was visible over the cerebral convexities. The lateral ventricles were greatly dilated ; the aqueduct was 0 4 cm. in diameter and the fourth ventricle moderately dilated. There was conspicuous haemorrhagic softening of the walls of both lateral ventricles,

especially in the occipital horns, and similar softening affected the bodies of both caudate nuclei, the lateral part of the head of the left caudate and the left optic thalamus, while a few punctate haemorrhages occupied both lenticular nuclei and the left internal capsule. In the body of the left ventricle the choroid plexus was swollen and purple; the right was less conspicuously affected. But in the temporal horns the plexuses appeared normal. Antemortem thrombus filled both the lesser veins of Galen.

Microscopical examination: There is no trace of organization in the antemortem thrombus filling the veins of Galen. The softening in the roof of the right lateral ventricle and in the left basal ganglia appears of recent date, being unaccompanied by any reaction on the part of the adjacent blood-vessels and macrophages. Many veins included in this area have undergone thrombosis, but the thrombus is completely unorganized. In the superficial cerebral veins adjacent to the superior longitudinal sinus there is early organization of the thrombus as shown by the occupation of peripheral parts by large mononuclear cells, and the adjacent leptomeninges are sparsely infiltrated with desquamated arachnoid cells and fewer neutrophil leucocytes. The choroid plexus from the body of the left ventricle shows great oedema and engorgement, many of the small vessels being distended with agglutinated red corpuscles. In a few places there is haemorrhage into the stroma of the tuft. The epithelial cells are plump and conspicuously vacuolated. In the left temporal horn the plexus is relatively anaemic and the epithelium is columnar.

In retrospect the histological investigation of this case was inadequate. At that time attention centred upon the thrombosis of the vein of Galen, which was tentatively regarded as the cause of the hydrocephalus. But thrombosis of the vein and its tributaries proved to be a terminal event and was ante-dated in the superficial cerebral veins. It is regrettable both that the superior longitudinal sinus was not examined microscopically and that no attempt was made to exclude the possibility of a coincidental basal meningitis. But the naked-eye appearances of the meninges and the distribution of the India ink both suggest that the meningeal pathways were open. It is difficult to conjecture how the thrombosis was initiated in this case: if the right otitis media was responsible, it is remarkable that the right lateral sinus should have been free from thrombus. But, again in restrospect, microscopical search for mural thrombi in this vessel should have been undertaken. Despite these obvious gaps in our information it appears most probable, from the clinical and pathological findings constituted together, that the hydrocephalus was due to diffuse cerebral venous thrombosis extending into or from the superior longitudinal sinus. The extension into the Galenic system, and the resulting venous infarction of the central tissues drained by these veins, was a terminal event.

The effects of thrombosis in the Galenic venous system are, in parenthesis, well demonstrated by the findings in a male infant (Reg. No. 30263/1936) of 3 weeks, the first child of its parents, who was admitted three days before death to the London Hospital with generalized convulsions, divergent squint and vomiting. Birth had been normal and the birth weight 8 lb. *On examination* there was retraction of the head and bulging of the anterior fontanelle, but no definite neck rigidity. Lumbar puncture yielded golden-yellow fluid under pressure containing red corpuscles and 1·6 per cent. of protein. At *necropsy* (P.M. 72/1936) the circumference of the head was 35 cm. There was a thin film of old greenish-brown haemorrhage in the subdural space in the right middle fossa and, less markedly, over the right parietal region. The torcular, straight sinus, great and lesser veins of Galen were all occluded by antemortem thrombus. The remainder of the dural sinuses contained fluid blood and postmortem clot. The ventricular system contained a cast of recent blood-clot and there was extensive haemorrhagic softening of the basal ganglia on both sides, accompanied by severe destruction of the ependyma throughout the greater part of the lateral ventricles. The late healing stages of this destructive process have been briefly mentioned in the case described on p. 8.

The following case, already reported in brief (1944), is a more instructive example of otitic hydrocephalus since it was more adequately investigated.

Case 47: E.P., *a male aged 15 years (Reg No. 31925/1938). He was a factory worker who* complained, on November 8th, 1938, of headache, vomiting and fever of sudden onset. Right otitis media was suspected but myringotomy was negative. On account of increasing drowsiness he was admitted to the London Hospital on November 26th.

On examination he appeared pale, ill and wasted. There was tenderness over the frontal *sinuses, especially on the right side.*

Nervous system: Papilloedema equivocal. Left pupil slightly larger than the right; both reacted sluggishly to light, but fully on convergence. There was a concomitant squint due to weakness of the external recti. The other cranial nerves were normal, though one observer recorded weakness of the left facial muscles. There was wasting and weakness of the left *upper limb, and especially weakness of dorsiflexion of the wrist, and he complained of pain* on hyperextension of the left fingers. There was weakness and slight spasticity of the left lower limb, most marked at the extremity. Thus there was almost complete paralysis of abduction of the foot and dorsiflexion of the ankle. The tendon reflexes were elicited as follows: supinator, right absent, left present; knee-jerks, both absent; ankle-jerks, right just present, left brisker; plantar responses, both sides flexor, though at a later date (unspecified) the left became extensor. Astereognosis was recorded, but sensation was otherwise unimpaired. Kernig's sign was positive. Further physical examination revealed bilateral pleural effusions and ascites, the result of extensive tuberculous infection.

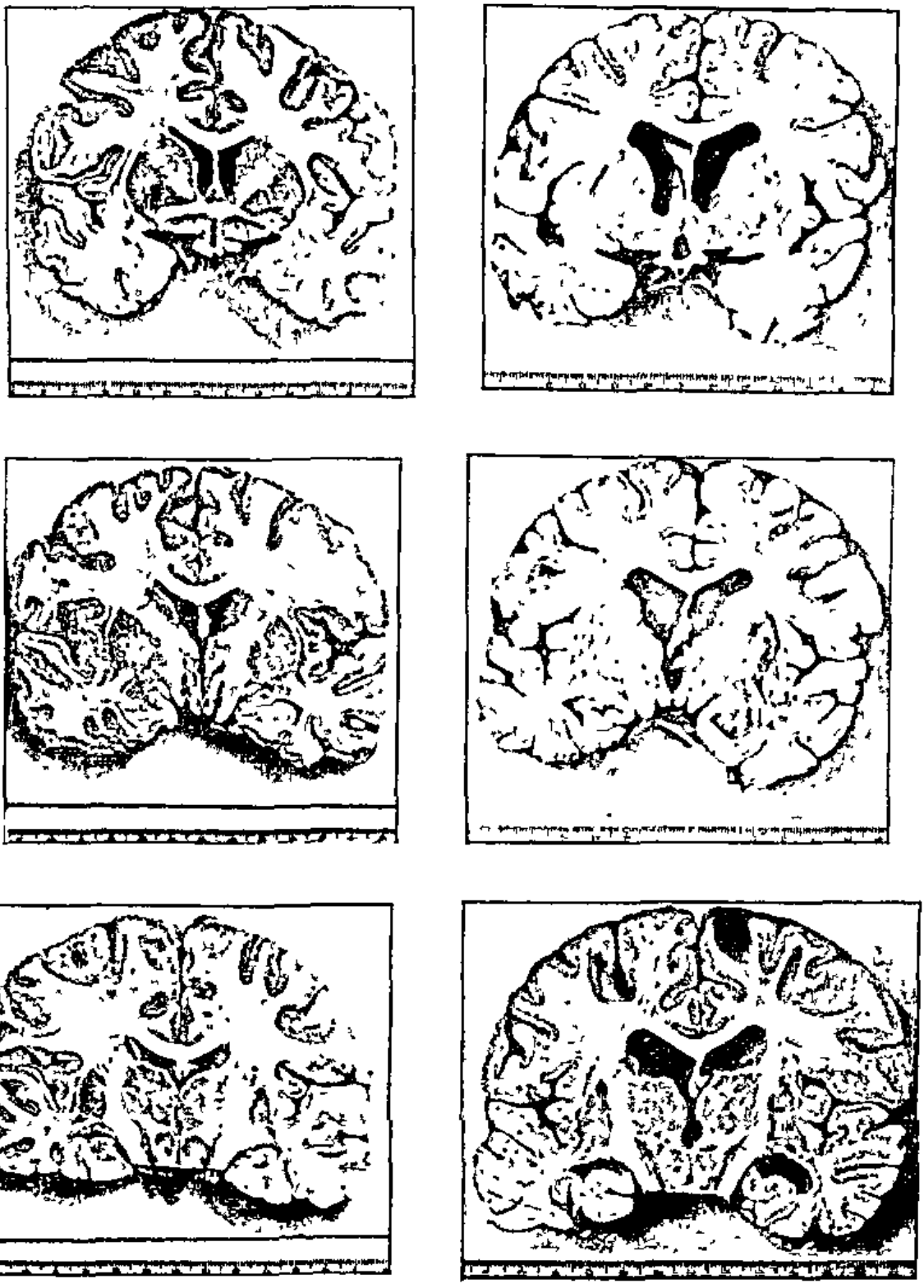
Lumbar puncture on the day of admission yielded 20 c c of clear fluid under a pressure of 220 mm, containing 20 mg of protein per 100 c c., and 1 cell per c.mm.; chlorides (as NaCl) 680 mg. per cent.; Wassermann reaction negative Specimens withdrawn on December 6th and 22nd were both sterile on culture

Progress: On November 30th the astereognosis had disappeared and there was improvement in the tone of the left upper limb and more power in the lower limb though there was still great weakness of the foot. The papilloedema had increased. Lumbar puncture yielded fluid under a pressure of 300 mm On December 20th papilloedema had further increased, especially in the right eye. On December 28th a special examination revealed no sign of disease in the right *ear, nor in the nasal and other accessory air-sinuses. By January 4th the papilloedema had* decreased, and at some date (unspecified) the 6th nerve palsy disappeared. The general condition of the patient steadily deteriorated and death took place on January 18th, ten weeks after the onset.

Necropsy. (P.M. 18/1938): The subject was a greatly-wasted, well-developed boy, in whom *death was due to perforation of a tuberculous ulcer of the ileum and chronic pulmonary* tuberculosis. Organizing thrombus occupied the whole length of the superior longitudinal sinus and of the right lateral sinus in continuity. In the latter there was macroscopic evidence of recanalization. The remaining dural sinuses appeared normal. Antemortem thrombus extended into many superficial veins over the cerebral convexities There was no flattening of the convolutions, and the leptomeninges appeared normal save for rusty pigmentation about the thrombosed veins. No excess of fluid was observed on the surface of the brain. On section a sharply defined area of greyish-brown necrosis, measuring 1 5 by 1·2 by 1 cm, *occupied the hind end of the right superior frontal convolution (Fig. 54). The ventricles were* slightly and symmetrically dilated, including the third ventricle. The aqueduct and fourth ventricle were not demonstrably dilated; the foramina in the latter were all patent. No evidence of tuberculous inflammation was found within the cranium. The right middle ear was moist; other accessory air-sinuses were normal.

Microscopic examination: The lumen of the right lateral sinus is occupied by organized thrombus with the exception of a space on either side of the central mass of granulation tissue. The collagen fibres in the latter are of variable calibre, but most are delicate, and many capillaries are present especially at the periphery. A good many red corpuscles are present outside the capillary lumina. There is no inflammatory reaction in the walls of the sinus. In the superior longitudinal sinus the centre of the thrombus is still unorganized, collagen being confined to the periphery and less dense than in the lateral sinus. No abnormality was detected in the arachnoid villi. The area of haemorrhagic infarction in the right cerebrum is *bordered by a well-defined zone of fat-granule and pigment macrophages, outside which is a* further zone of early gliosis. The adjacent cerebral veins are thrombosed, but organization in them is little advanced. There is no histological abnormality in the meninges about the medulla oblongata and the foramina of Luschka.

In this case we have evidence that aseptic sinus thrombosis, presumably of the marantic type, began in the right lateral sinus and spread backwards into the superior longitudinal sinus, since organization is less advanced in the latter situation. The thrombosis also extended into the superficial cerebral veins, and was evidently complicated by slight focal subarachnoid haemorrhage at an



Control Sections *Case* 47

FIG 54: *Case 47.* Coronal sections of brain with corresponding level from a normal control arranged on left. Note ventricular dilatation and infarct in right frontal region in lowest section from Case 47, as described in the text. (By kind permission of the Editors, *Proceedings of the Royal Society of Medicine*)

early stage, as shown by the presence of rusty pigmentation along these vessels at necropsy. The left-sided paresis was accounted for by the parasagittal haemorrhagic infarct in the right frontal lobe, and this must have been present at the time of admission to hospital, eighteen days after the onset of the illness. From the clinical records it appears that the intracranial pressure increased after admission, but the degree of papilloedema present suggests that it was declining just before death. The latter was due to perforation of a tuberculous ulcer of the small intestine and not to the intracranial condition which, it may be surmised, was gradually subsiding. The degree of internal hydrocephalus observed was admittedly slight and, had the brain been sliced while still unfixed, might easily have been passed as normal. This point is worth noting because it is by no means clear that some of the cases of this kind already published have been critically examined for the presence of lesser degrees of ventricular dilatation.

Case 48: B W., female aged 20 (Reg No. 21383/1946) At the age of 7 she had pneumonia, for the treatment of which "they collapsed her lung" but did not tell her mother whether tuberculosis was diagnosed She remained fairly well until the age of 13 when she contracted rheumatic fever and, one year later, became ill again with alleged "chronic rheumatism" At this time her mother noticed that swelling of the limbs, legs and face occurred and lasted for days. She complained too of continual headache, and of double vision if anything or anybody came too near her. Thirstiness and frequency of micturition were also noted These symptoms continued intermittently up to her final illness, but she was able to work as a machinist during remissions. There was no history of ear infection at any time Four months before death her mother noticed that she limped, and three days later, on attempting to get up in the morning, the right arm and leg felt dead and she could not move them On the same morning the left side of the face became paralysed and she complained of severe headache. On admission to another hospital, three days later, she was fully conscious but suffered from headache, double vision and occasional vomiting In this hospital the cerebro-spinal fluid, a few days after admission, contained 30 mg of protein per cent with no excess of globulin ; 6 white cells per c.mm. ; and was sterile on culture. Later (nine days before death) the protein had risen to 80 mg. with slight excess of globulin, and white cells were 47 per c mm. (70 per cent. polymorphonuclear leucocytes and 30 per cent lymphocytes) ; cultures sterile. The *blood* examined 10 days after the first lumbar puncture showed a leucocytosis of 14,400 of which 73 per cent. were polymorphonuclear and 22 per cent lymphocytes.

Sixteen days before death she became unable to speak and later became drowsy. On admission to the London Hospital, one day before death, she was deeply unconscious, breathing noisily: temperature, 101° F. ; pulse, 120 Left-sided proptosis and ptosis were present, and partial ptosis on the right. There was divergent squint with rapid nystagmoid movements of both eyes ; corneal reflexes were sluggish. There was spasticity of the right arm ; both arms moved in response to painful stimuli. Both legs were flaccid and there was a right extensor plantar response. B.P. 135/90 Moist râles were present in the chest.

Ventriculography was performed to exclude abscess. Both ventricles were entered with ease. Pressure 90 mm. ; clear colourless fluid Lumbar puncture pressure of 470 mm. reduced to 200 mm. after ventricular tap. She died in hyperthermia on the following day. Left ventricular fluid was clear and colourless, and contained 20 mg. of protein. *Lumbar fluid* 880 red cells and 8 white cells per c.mm. (90 per cent. lymphocytes) ; 50 mg. per cent. of protein ; sterile on culture.

Necropsy (P.M. 335/1946): *Bronchopneumonia. Focal encephalitis of mid-brain, pons and hypothalamus: Recanalized thrombosis of dural venous sinuses*

A well-nourished and well-developed woman. Obliteration of pericardial sac by old relatively avascular easily-broken fibrous adhesions Slight atrophy of myocardium. Valves normal. Slight atheroma. Fibrous adhesions obliterating greater part of both pleural cavities. No evidence of tuberculosis in lungs or in bronchial lymph-nodes Slight chronic bronchiectasis without adjacent fibrosis in lower lobe of left lung. Broncho-pneumonia in lower lobe of right lung. Oedema of lungs. Parenchymatous degeneration of liver and kidneys. Slight sub-acute inflammation of pulp of spleen. Slight diminution of lipoid in cortex of suprarenal bodies.

Central nervous system:

Macroscopic examination: The lumina throughout both lateral sinuses were occupied by pale pinkish-grey fenestrated fibrous tissue. A separate localized segment (about 3 cm. long) of similar appearance occupied the superior longitudinal sinus opposite the junction of the parietal and occipital lobes. The straight sinus was patent but its lumen constricted (about 0·15 cm. in diameter) and enclosed by milky-white fibrous tissue. The other dural sinuses appeared normal. The middle ears, mastoids, nasal and other accessory sinuses were normal.

The surfaces of the brain appeared unaltered: there was no evidence of old or recent thrombosis of the cerebral veins. On section there was slight symmetrical dilatation of the lateral ventricles, shown by fullness of the anterior horns and rounding of the lateral angles of the bodies (slightly less than that shown in Fig. 54 of Case 47). Pinkish-grey softening affected the ventral part of the anterior end of the pons, involving the left side more than the right but extending to the right at the level of the middle cerebellar peduncles Less definite softening extended upwards into the left crus. The medulla, cerebellum and spinal cord appeared normal save for pearly-white degeneration in the site of the right crossed pyramidal tract throughout the cord.

Microscopic examination Transverse sections through both lateral sinuses, the affected part of the superior longitudinal sinus and the straight sinus show in all an antecedent thrombosis which has become organized by fibrous tissue and extensively recanalized (Fig 55). The tissue is free from cellular inflammatory infiltration, and fibrocytes are scanty. Sections from representative parts of the brain, and others taken serially from the brain-stem, show no change above the level of the hypothalamus Here there is perivascular cuffing of a few vessels with small lymphocytes. This becomes more conspicuous in the mid-brain, especially in the region of the crura cerebri, where there is extensive ill-defined softening, especially on the left. In the softened areas demyelination is great, but uneven and ill-defined; it is associated with numerous foam cells and a reaction of the astrocytes which are slightly increased in number and greatly swollen In a few areas considerable infiltration with polymorphononuclear leucocytes is found, in places forming minute purulent areas. This destructive inflammatory process extends caudally into the pons, being limited to the basal half, and ends abruptly at the level of the middle cerebellar peduncles. There is no leucocytic infiltration, however, in the pons. Below this there is no histological change apart from a unilateral descending pyramidal degeneration. The meninges are little affected but, in the region of the encephalitis, there is a sparse uneven lymphocytic infiltration without fibrosis. The meningeal vessels appear normal

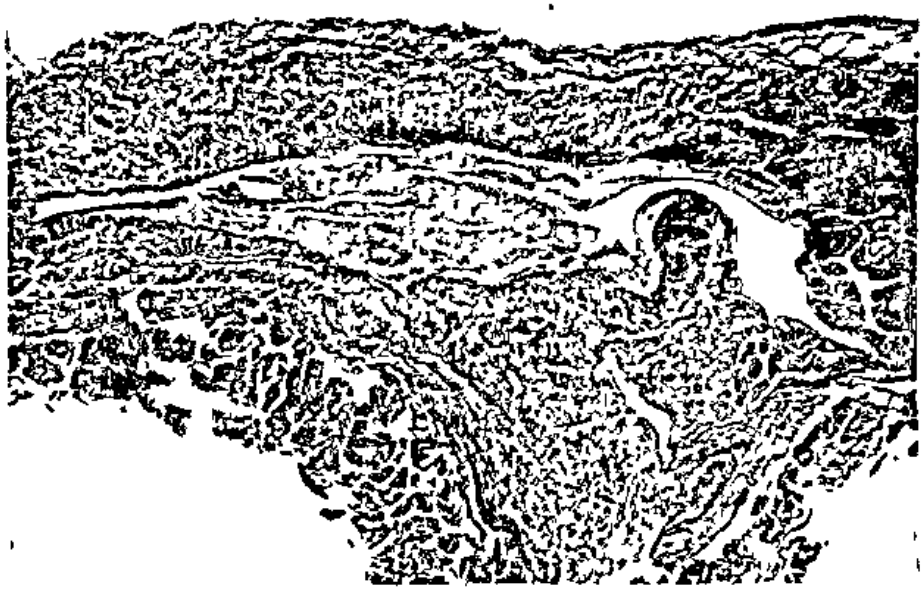


FIG. 55. *Case 48*: Transverse section of superior longitudinal sinus. The lighter central area represents organized, recanalized thrombus van Gieson. × 13 5

It is particularly unfortunate that in this case the picture of dural sinus thrombosis has become irreparably blurred by a terminal encephalitis. Although interpretation thus calls for considerable caution it may be fairly assumed that the encephalitis developed four months before death, at the onset of the right-sided weakness, whereas the sinus thrombosis was considerably older. There is no clear clinical evidence of the date of this earlier event though the story of severe headache and diplopia occurring seven years before death is

suggestive, particularly in association with oedema of the face and extremities which may have been referable to multiple thromboses since there was no anatomical evidence of an antecedent nephritis. The sinus thrombosis was of greater age than in Case 47 (p. 89) and had become completely organized and recanalized. Again, as in Case 47, there was a slight degree of ventricular dilatation, but here the possibility must be entertained that this dilatation was secondary to the encephalitis. Weight is added to this alternative by the observation of increased pressure of the cerebro-spinal fluid at the lumbar level. No explanation can be offered for the simultaneous low ventricular pressure, for there was no anatomical evidence of any block within the vertebral canal. This case has been considered worthy of record in spite of these difficulties of interpretation, since it provides a late picture of dural sinus thrombosis and at least shows that, if dilatation of the ventricles persists, the degree is so slight that it might easily be missed.

In Case 1 described by Bailey and Hass (1937) the papilloedema had receded during the month before death though it had not completely disappeared. At necropsy a moderate symmetrical dilatation of the lateral ventricles was associated with organized and canalized thrombus throughout the posterior two-thirds of the superior longitudinal sinus and the right lateral sinus. The child had apparently died from other causes, and it may be assumed that the intracranial disturbance was subsiding. But there is no evidence in this case, or in Case 47, to suggest that the size of the ventricles had decreased with the fall in intracranial pressure. Yet this possibility must be entertained in view of the interesting observation made by Scarff (1942) in his Case 4. In this, a female infant aged two months, suffering from a lumbar meningocele and internal hydrocephalus, was treated by endoscopic cauterization of the choroid plexuses. Ventriculography was performed at the time of this operation, and again 15 months later; the results showed a conspicuous diminution in the size of the ventricles during this period. That a dilated ventricle can contract when operative measures have relieved pressure has been shown by Cairns *et al.* (1947) in their report on localized hydrocephalus following penetrating wounds of the ventricle. In their first case encephalography one month after operation showed the dilated part to be "much reduced in size", while in the second case, after one year, it was "normal in size and position". Though little is known of the potential elasticity of the ventricles it may well be found that, in cases of so-called otitic hydrocephalus, the ventricles undergo a phase of expansion while intracranial pressure is mounting and return to their normal size as the thrombus becomes canalized and pressure falls.

Another possibility should be mentioned in connection with certain published cases of increased intracranial pressure associated with sinus thrombosis in which the ventricles, at necropsy, have been described as normal, or small. In these cases the pathologist is apt to remove the brain with its dural covering and to fix the whole en masse. Unless the brain has been perfused with formaldehyde through the arteries the fixation of the central parts of the brain in these circumstances is poor, and the ventricles tend to collapse. In personal experience of an instance of this kind it was found that the ventricles had become so small that it was difficult to credit the clinical claim of advanced hydrocephalus. But a ventriculogram, taken a few days before death, left this question in no possible doubt. It is difficult not to draw an analgous conclusion in reading a case report such as that by Keschner and Davison (1942) in which, nine days before death, encephalography had revealed well outlined and

symmetrically dilated lateral and third ventricles, whereas photographs of two coronal sections of the brain show no such dilation.

And now, having set forth a certain amount of evidence pointing to the development of internal hydrocephalus as a result of dural sinus thrombosis, we must admit that experimental attempts to reproduce this syndrome in laboratory animals have signally failed (Beck and Russell, 1946). The various means adopted in an attack upon the superior longitudinal sinus have belied the reputation attached to this vessel for ease of spontaneous thrombosis. And, without entering into a catalogue of all the different expedients which were tried, for details of which the reader is referred to the original paper, it was ultimately found that the greater part of the sinus could be completely obliterated in both young and adult animals, by packing the lumen with cotton wool, without any subsequent impairment of normal function. All these animals enjoyed perfect health and activity until killed at intervals of up to seven weeks later, and at no time was papilloedema observed. In most instances no ventricular dilatation was found on examining the brain; in a few only slight and equivocal degrees were present. Evidently the collateral circulation could at once compensate for the operative disturbance. Reparative processes, ending in the organization and recanalization of the occluding material were quickly initiated. While it is difficult to reconcile these results with the syndrome of otitic hydrocephalus in man, it may be that it is necessary for the occluding thrombus to extend from the main lumen of the sinus into the adjacent lacunae and the mouths of the venous tributaries in order to bring about a gross disturbance in the absorption of the cerebro-spinal fluid and a consequent rise in intracranial pressure. If this be true it would explain why otitic hydrocephalus complicates only a certain proportion of the instances in which sinus thrombosis follows otitis media. It would also explain why Dandy (1940) and Jaeger (1942) found it possible to resect considerable lengths of the longitudinal sinus during the removal of parasagittal tumours without incurring any untoward clinical disturbances.

CHAPTER VI

NEOPLASMS

THE number of cases in which a neoplasm has been responsible for the development of internal hydrocephalus forms a large percentage of the present series. It would be incorrect, however, to assume that this preponderance is representative of hydrocephalus in the population as a whole: it is clearly the result of the writer's association with active neurosurgical departments. Little would be gained by the presentation of this rather bulky material as separate cases, since much would be purely repetitive. It is proposed therefore, with certain exceptions, to condense the experience acquired in this group into a more general account.

Tumours of the Cerebral Hemispheres

Within the cerebral hemispheres the general rule holds that constriction or obliteration of the lumen of the lateral ventricles will lead to dilatation of such parts as are thereby cut off from the foramen of Monro. Thus a tumour occluding the body of the ventricle will be accompanied by dilatation of the occipital and temporal horns on the same side. Quite commonly a glioma in the region of the anterior part of the corpus striatum, the Island of Reil or temporal lobe, will cause so much lateral dislocation of the ventricular system as a whole that the foramina of Monro are almost blocked, and the third ventricle greatly compressed (Fig. 56). Then not only are the occipital and temporal

FIG. 56: Spongioblastoma multiforme of right temporal lobe, showing distortion of ventricular system and dilatation of anterior horn on opposite side (P.M. 153/1932)

horns dilated on the same side as the tumour, but the ventricle of the opposite side may show a more or less generalized dilatation which, in the case illustrated, was conspicuous in the frontal horn. Again tumours of the cerebrum may cause compression of the aqueduct as the result of herniation of the ipsilateral hippocampal gyrus through the tentorial opening. The herniated tissue presses upon the crus and lateral aspect of the mid-brain with the result that the

FIG. 57: Compression of aqueduct by tentorial herniation of right hippocampal gyrus (P.M. 153/1938)

aqueduct is narrowed to a slit (Fig. 57). This might be expected to cause increased dilatation of the lateral ventricles but, in most examples, this deformity of the brain appears to be a swift terminal event and little dilatation may be observed. But inequality of pressure above and below the tentorium in five such cases was demonstrated by Smyth and Henderson (1938) by taking simultaneous readings of the intraventricular and spinal fluid pressures. They found that the intraventricular readings were from 20 to 100 mm. of water higher than the spinal. Postmortem proof of herniation of the ipsilateral hippocampus was obtained later in all cases, and it appeared that obliteration of the aqueduct was responsible for the inequality of pressure.

Tumours of the Third Ventricle

Tumours occupying the cavity of the third ventricle will cause a symmetrical enlargement of both lateral ventricles. A good example is provided by the "colloid cyst", a small globular tumour attached to the choroid plexus opposite the foramina of Monro which, by its mobility, causes intermittent attacks of hydrocephalus by acting as a ball-valve in this situation (Fig. 58). A variety of tumours arising within or compressing the third ventricle may produce a similar dilatation, such as the suprasellar Rathke-pouch tumour (or craniopharyngioma), chromophobe adenomas of the pituitary gland, glioma of the

basal ganglia and so forth (Fig. 59). Ependymal gliomas arising further back in the ventricle may effectively plug the opening of the aqueduct with a resulting dilatation of the third as well as of the lateral ventricles.

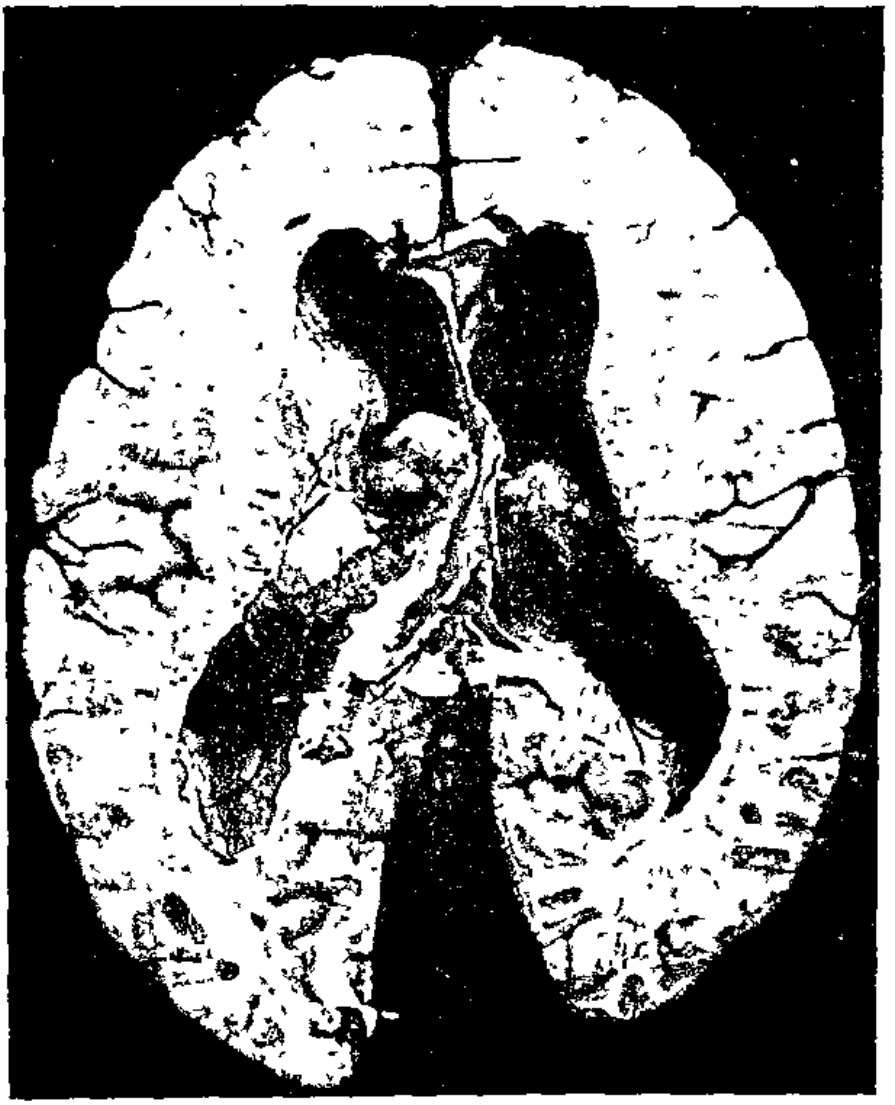


FIG. 58: Colloid cyst of third ventricle, protruding through left foramen of Monro

Tumours of the Mid-Brain

In the region of the mid-brain the aqueduct may be obstructed by tumours outside the brain-stem as well as by those which compress or occlude the lumen through growth within the neural tissue itself. Thus tumours of the pineal body are apt to embed themselves in the quadrigeminal plate, with or without actual invasion of the tissue, and thereby compress the aqueduct from above. Aneurysms of the great vein of Galen act in a similar fashion. A remarkable example of the latter (Fig. 60) has been described in detail elsewhere (Russell and Nevin, 1940) together with a second example that came to necropsy at the London Hospital in 1921. Both were in young infants and were clearly congenital malformations. Another similar example has since been described by Alpers and Forster (1945).

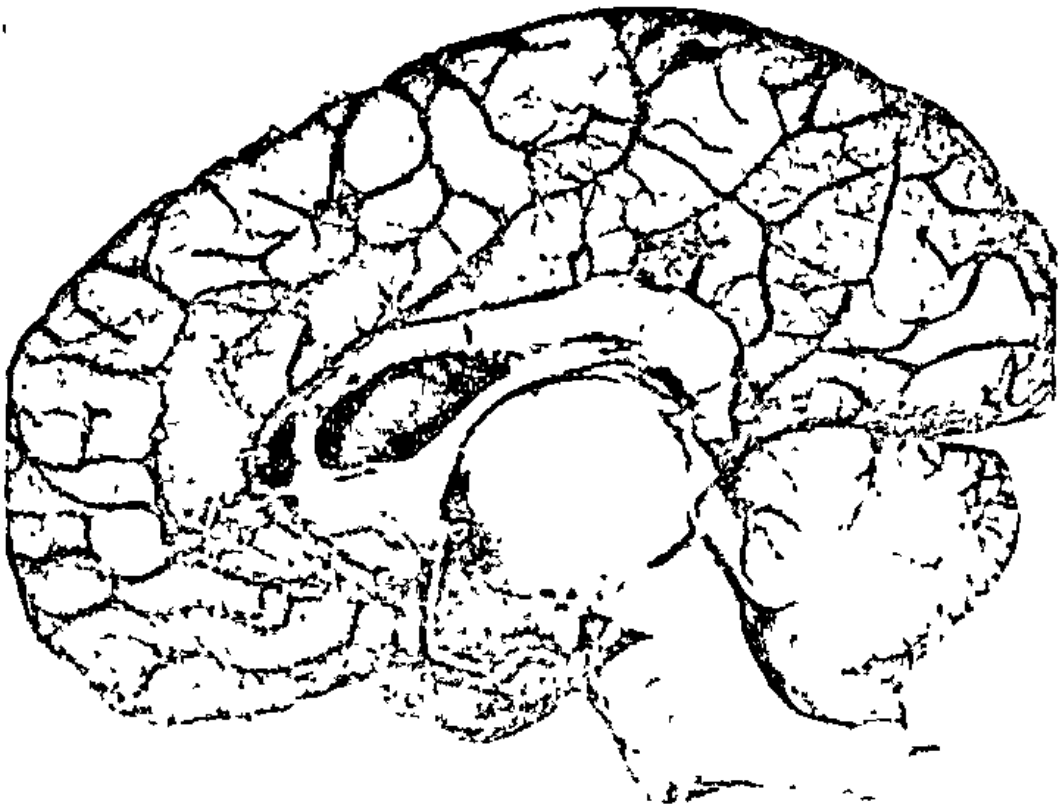


FIG. 59. Astrocytoma arising from basal ganglia and occluding greater part of third ventricle

The only common tumour of the mid-brain itself is the astrocytoma, and five examples of this kind are included in the present series. Occasionally the glioma forms an extension of a larger mass in the basal ganglia on one side, especially in the region of the pulvinar, which infiltrates the crus and finally encroaches on the aqueduct. A remarkable instance of this was found in an infant aged 1 year (London Hospital, P.M. 501/1922). The child's head began to expand at the age of 4 months and reached a circumference of 57 cm. Macroscopically the aqueduct appeared to be occluded just behind the third ventricle which, with the lateral ventricles, was grossly dilated. The fourth ventricles and meninges were normal. Microscopically the aqueduct was greatly narrowed and distorted by a diffuse astrocytoma extending from the pulvinar into the quadrigeminal plate and lateral border of the mid-brain.

When the astrocytoma is confined to the mid-brain the distinction between this lesion and "gliosis" of the aqueduct (p. 41) may not always be easy histologically, and clinically the separation may be impossible. The five examples of the present series were all in young subjects, three being in children. Though it might be expected that the cases in which a tumour was present would run a more rapid course than in "gliosis" the evidence does not bear this out.

Thus the example illustrated in Fig. 61 was in a boy of 6 years with a history of neurological disturbance dating back to the age of 2.* At this time his head was already enlarged, and he began to suffer from headaches and lost the power of walking. In the later stages he became markedly spastic and developed papilloedema. At necropsy the quadrigeminal plate was found to be converted into a cushion-like mass of firm, rubbery white tissue (Fig. 61) which, microscopically, was composed of a dense tangle of fibrillary astrocytes.

* I am indebted to Dr. Douglas McAlpine for the clinical history in this case.

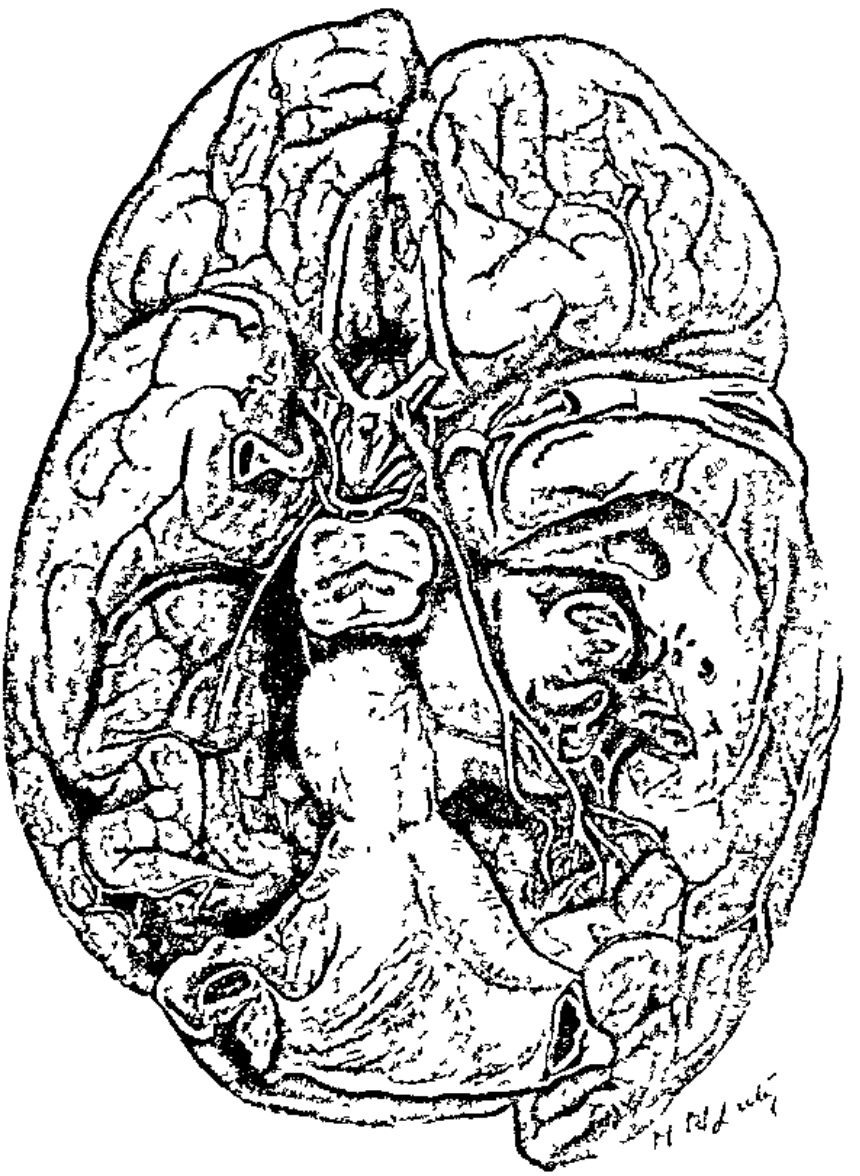


FIG 60: Complex arterio-venous hamartoma including aneurysm of great vein of Galen compressing quadrigeminal plate. Considerable internal hydrocephalus was present. (By kind permission of the Editor, *Journal of Pathology and Bacteriology*)

At one point, about the centre of the aqueduct, the tumour crossed the lumen to infiltrate the floor. The fourth ventricle, as would be expected, is seen in the photograph to be of normal size.

FIG 61: Astrocytoma of quadrigeminal plate causing stenosis of aqueduct

The example just quoted is clearly neoplastic. That now to be described presents difficulties in interpretation, and might be regarded alternatively as a case of gliosis of the aqueduct.

Case 49· M.D., a boy of 15 years (Reg. No. 11004/1938). He had developed normally until the age of 7 to 8 years when he was noticed to drag his right foot. In retrospect it was said that he had always been "bad on his legs". Walking then became progressively more difficult but he remained at school until the age of 12 and was said to have been an exceptionally good scholar. By the age of 13 to 14 he was unable to stand, his hands, especially the right, became weak and tremulous and he began to suffer from occasional severe headaches He increased in weight, and had a large appetite but no excessive thirst During the last 12 months control of bowels and bladder became poor.

On examination he was a fat, dull-looking placid boy 6 ft. 1 in in height and weighing 12 st 11 lb. The obesity was mainly of the trunk and neck. Secondary sex characters were normally developed except that the distribution of pubic hair was of feminine type and axillary hair was scanty. Speech was slow but there was neither dysphasia nor dysarthria. His head was enlarged, measuring 67 cm. in circumference. No abnormality was present in the cranial nerves and the discs were flat and pale. All limbs were weak, with increased tendon reflexes especially on the right. Ankle clonus was present, most marked on the the right and both plantar responses were extensor. There was some defect in joint-sense in the right lower limb and tactile discrimination was impaired in both right limbs. Blood pressure 140/100 mm. Hg

X-ray of the skull showed enlargement of the pituitary fossa and loss of the posterior clinoid processes. Well-marked convolutional impressions were present over the vault.

Lumbar puncture yielded colourless fluid containing 60 mg per cent of protein and 8 white cells per c mm. The Wassermann reaction was negative, and the Lange curve 0012200200.

Sugar tolerance curve· Fasting blood sugar was 0 190 per cent. Fifty grams of glucose were then given· subsequent levels of the blood-sugar at hourly intervals were 0 250, 0 166 and 0 166 per cent. No specimens of urine were obtained.

Ventriculography showed great enlargement of the third and lateral ventricles. The aqueduct was not visualized. Ventriculostomy through the anterior wall of the third ventricle was followed by death in hyperthermia on the day after the operation

Necropsy: (P.M. 169/1938): *Internal hydrocephalus Stenosis of aqueduct.* No significant changes were present in the rest of the body. The endocrine glands were of normal macro- and microscopic appearance. The testes, though small, showed spermatogenesis. There was marked fatty infiltration of the liver.

The *skull* showed great thinning of the vault with translucency of the frontal and parietal regions. The base was flattened and the pituitary fossa greatly expanded, measuring 2·3 by 2·3 cm. and 1·2 cm. deep. There was no abnormality of the leptomeninges, nor of the external surfaces of the brain beyond fullness of the cerebral hemispheres and the presence of an operation opening in the anterior wall of the third ventricle.

On section there was gross dilatation of the third and lateral ventricles with much fenestration of the septum pellucidum. The ependyma was everywhere smooth and glistening. The aqueduct rapidly narrowed to a pinpoint orifice, measuring 0·05 cm. from side to side and less than 0·05 cm. from above down, beneath the anterior corpora quadrigemina. A fine horse-hair could be passed through it. Below the posterior corpora quadrigemina the lumen again expanded to normal dimensions and the fourth ventricle was undilated.

Microscopic examination In a transverse section through the hind end of the anterior corpora quadrigemina (Fig. 62) the aqueduct is greatly reduced and deformed. A few small nests of ependymal cells are present in each lateral angle and, at the ventral angle, a short interrupted row of small groups of these cells descends vertically into the median raphe. The remainder of the lumen is lined with fibrillary neuroglia. There is no excess of this tissue, however, except dorsal to the lumen where a spherical mass of neuroglial tissue with a conspicuous concentric arrangement of the fibrils lies in close relation to the lumen. This mass is rather sparsely cellular. Many of the nuclei are abnormally large and of bizarre form. There is no cellular inflammatory infiltration. The leptomeninges at the base contain a little recent haemorrhage and slight polymorphonuclear infiltration attributable to the operation.

Fig. 62: Case 49. Transverse section through hind end of anterior corpora quadrigemina (see text). Phosphotungstic-acid haematoxylin × 14·5

It is open to debate whether the neuroglial tissue causing the constriction of the aqueduct in this case is of the nature of a neoplasm, or of the character already described when considering gliosis of the aqueduct (p. 47). While the clinical history seems disproportionately long in comparison to the amount of neuroglial proliferation demonstrated, little is known of the variations in speed of growth of the fibrillary astrocytomata. The peculiar configuration of the neuroglia in the quadrigeminal plate, and the character of the included nuclei are both suggestive of neoplastic activity. Whatever the correct solution, this case, taken in conjunction with that just previously described, illustrates the *difficulties in separating the two conditions, and the identical character of the* clinical picture.

Other tumours, such as lipomata and angiomata, of the nature of hamarto-

mata rather than true neoplasms, may arise in the substance of the mid-brain but they are very rare. Fig. 63 shows in sagittal section part of an extensive arterio-venous hamartoma in a boy of 16 years. It involved the anterior part of the mid-brain and left thalamus and was associated with gross internal hydrocephalus.

FIG. 63. Arteriovenous hamartoma (serpentine angioma) of mid-brain and left thalamus with severe internal hydrocephalus

TUMOURS PROJECTING INTO THE LUMEN OF THE AQUEDUCT

Reference has already been made (p. 19) to berry aneurysms, and to tuberculomata (p. 83) in this situation. Apart from the stenosis caused by neoplasms of the quadrigeminal plate it occasionally happens that a minute tumour projects into the lumen, thereby causing severe internal hydrocephalus. Such a picture is presented by the following case, in which a polypous *astrocytoma of small size was attached to the posterior commissure.*

Case 50 M F, a female aged 19 years (Reg. No 41047/1923) She had suffered for the preceding four years from severe headache, noises in the ears, attacks of vomiting and amenorrhoea. The headaches were relieved by retraction of the head For the preceding two months she had had frequent attacks in which her eyesight failed, her legs gave way and she lost consciousness On examination she was a fat, emotional girl with a vacant expression and of poor intelligence. Axillary and pubic hair was scanty. The fundi showed blurring of both discs A fine lateral nystagmus was present, and occasional strabismus on attempting to focus the eyes There was slight paresis of the right side of the face Spasticity of the lower limbs and extensor plantar reflexes were the only other abnormal signs noted Death took place a week after a bi-temporal decompression had been performed
Necropsy (P M. 230/1923) *Hydrocephalus Occlusion by polypous glioma of aqueduct* Purulent bronchitis. Fibrous adhesions obliterating right pleural sac. Small colloidal adenoma in right lobe of thyroid gland Small amount of glandular tissue in thymus. A well-developed, fat girl. No other significant changes were noted except in the brain.
Examination of brain Bilateral hernia cerebri at sites of operation. Great enlargement of sella turcica, erosion of the posterior clinoid processes and flattening of the pituitary body and

of the sphenoidal air-sinus. Great bulging of the floor of the third ventricle. One pint of clear cerebro-spinal fluid was obtained from the lateral ventricles There was no evidence of meningitis. A sharply defined pale yellow polyp, 0 5 cm. long and 0 2 cm. in diameter, attached to the centre of the inferior surface of the posterior commissure, filled the anterior end of the aqueduct.

Microscopic examination The polyp (Fig 64) is composed of dense fibrillary neuroglia with a concentric arrangement of the fibres, and few cells, most of which lie near the centre. It occupies the roof of the aqueduct, the lumen of which is spread out as a crescent beneath it. There is no cellular inflammatory infiltration in the neighbouring tissues.

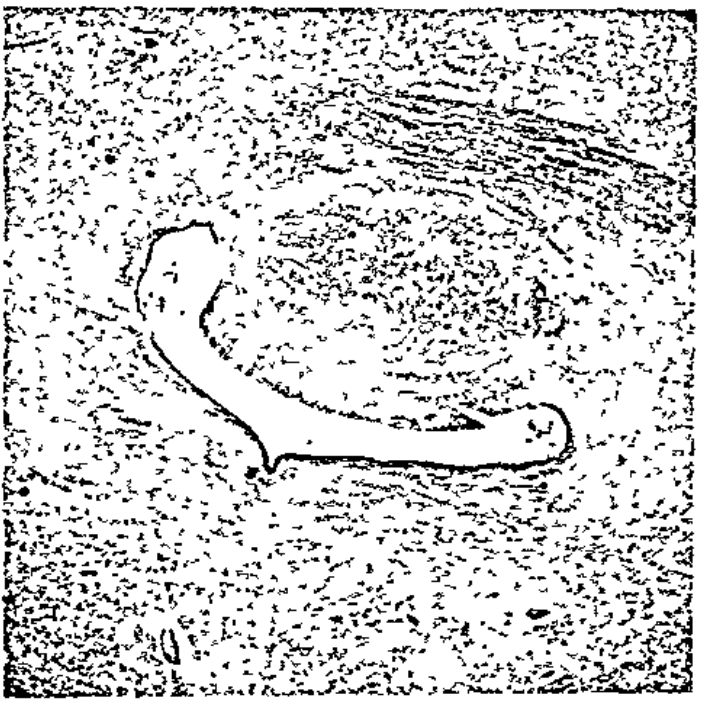


FIG. 64: *Case 50:* Transverse section through anterior end of aqueduct. For details see text. H. and E. × 15

This case, like that just described, illustrates the development of a Fröhlich's syndrome from slowly progressive pressure in the infundibular region. The histological character of the causative lesion in both is remarkably similar, the only essential difference being the relationship of the mass to the lumen of the aqueduct.

Tumours of the Fourth Ventricle

The cavity of the fourth ventricle may be occluded by such tumours as papilloma of the choroid plexus, or ependymoma, with similar effects upon the ventricular system, which is uniformly dilated anterior to the site of occlusion. *Likewise cerebellar tumours, especially the medulloblastoma, may occlude the* ventricle by direct extension (Fig. 65). Astrocytomata and haemangioblastomata of the cerebellum are less liable to occlude the main cavity of the ventricle, but they not infrequently abut on the hind end in the region of the foramen of Magendie, with corresponding obstruction to the circulation of the cerebro-spinal fluid (Figs. 66 and 67). The tumour shown in Fig. 68, a small ependymoma attached by a narrow pedicle to the medulla in the region of the area postrema, was an accidental finding at necropsy in a man of 58 who died from ascending purulent pyelo-nephritis. The tumour occluded the foramen of Magendie and was responsible for a slight dilatation of the ventricles (Fig. 69). The foramina of Luschka appeared to be patent.

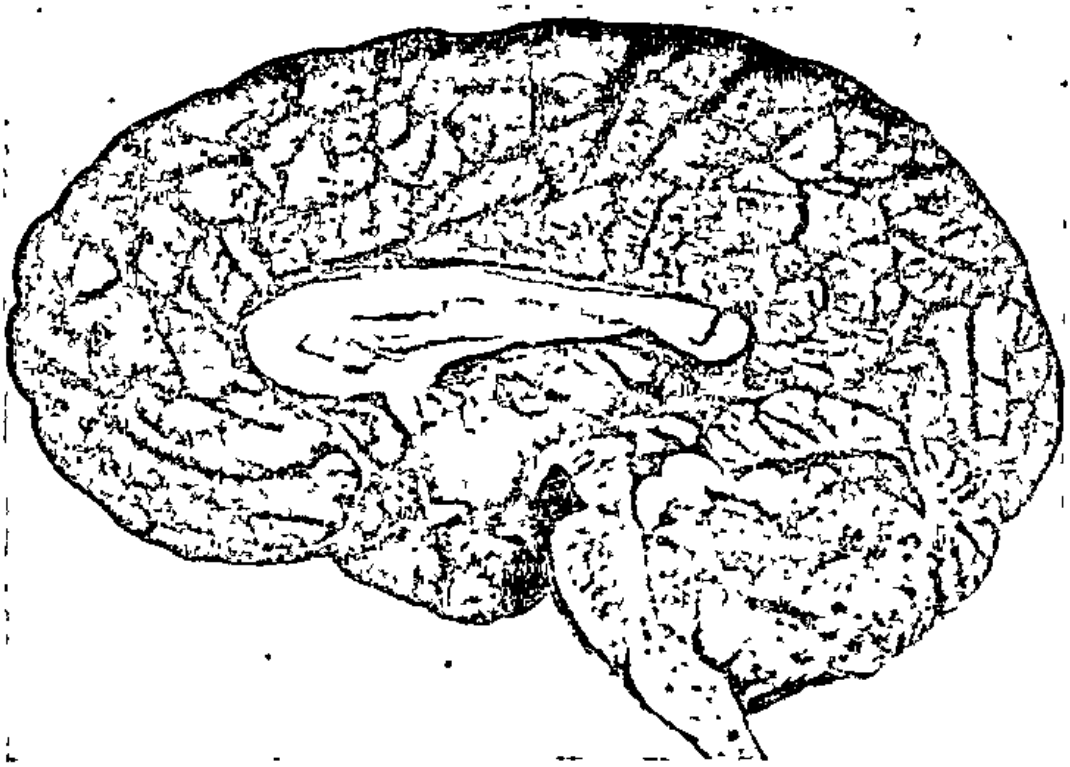


FIG. 65: Medulloblastoma of cerebellum occluding fourth ventricle

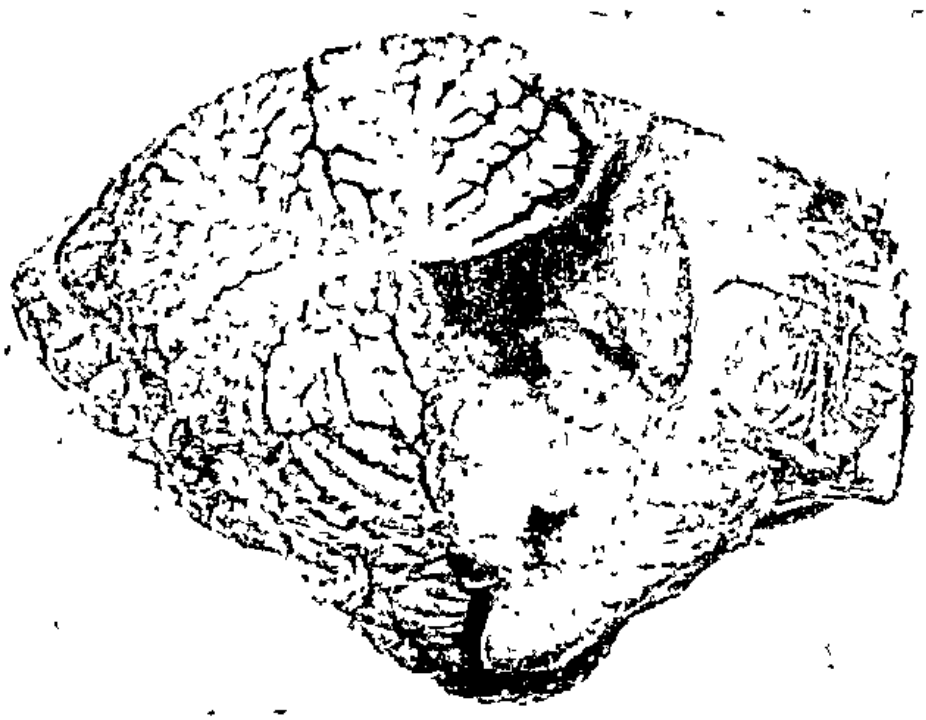


FIG. 66: Astrocytoma of hind end of fourth ventricle

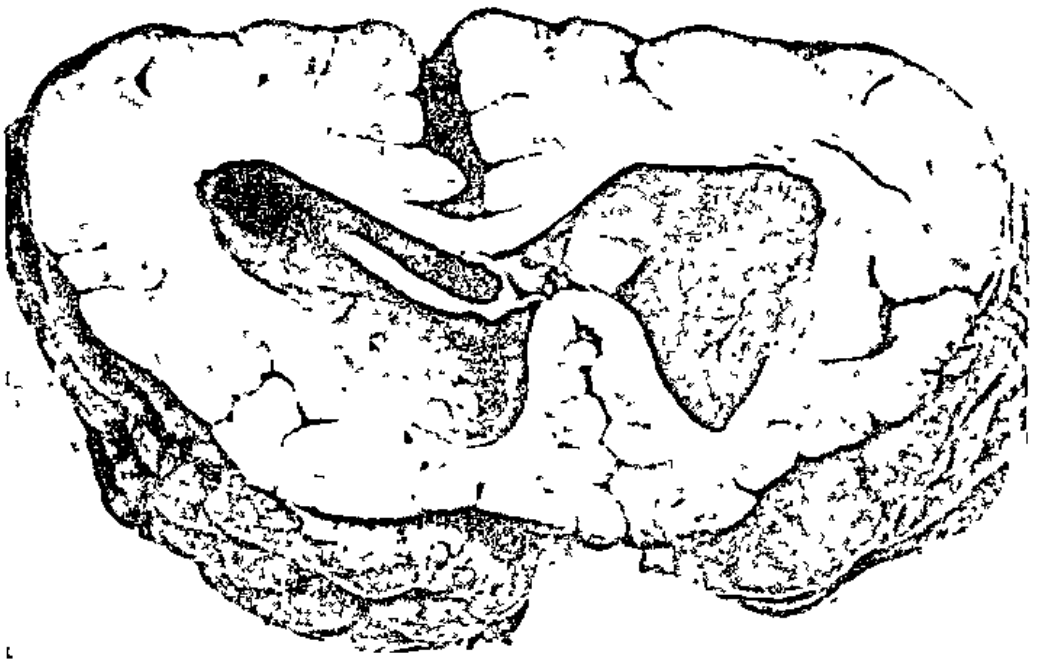


FIG. 67: Coronal section of cerebrum showing the hydrocephalus caused by the tumour illustrated in Fig 66

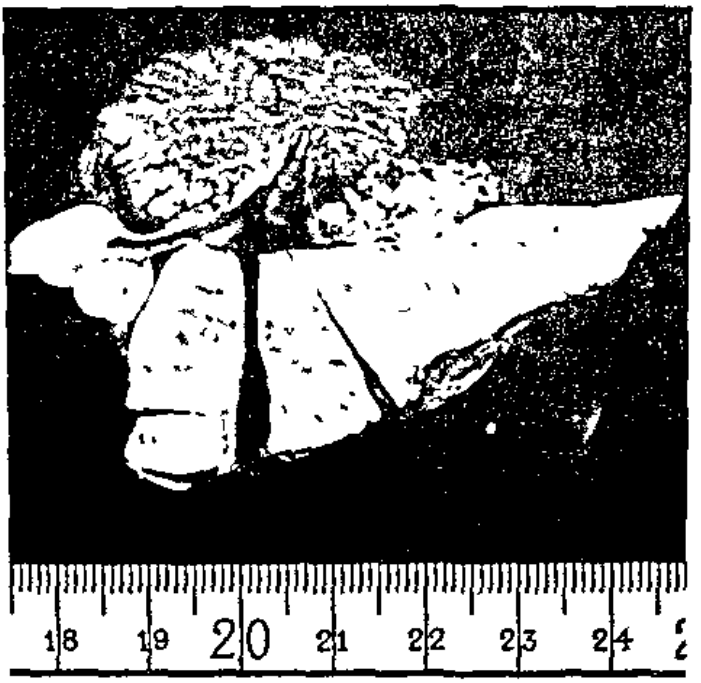


FIG 68: Ependymoma occupying foramen of Magendie (P.M. 26/1946)

FIG 69: To show the slight degree of hydrocephalus caused by the tumour in Fig 68

Cerebellar and Ponto-Medullary Tumours

Astrocytomata of the cerebellum, the diffuse pontine and medullary-pontine tumours which are almost invariably astrocytomata, the cerebello-pontine tumours and other space-occupying lesions of the posterior fossa may cause hydrocephalus by more than one mechanism. They may deform and even partly occlude the lumen of the fourth ventricle or the hind part of the aqueduct (Figs. 70 and 71), but, from the examination of a large series of cases, this seems a less potent and common cause than the effects created by extensions of the tumour into the leptomeningeal spaces, thereby occluding the cerebro-spinal pathway through the basal cisterns and tentorial opening. Thus it is often found that the fourth ventricle, though greatly deformed, is enlarged rather than reduced (Fig. 22, p. 39). The photograph shown in Fig. 72 gives some idea of the degree of hydrocephalus which accompanies a cerebello-pontine tumour.

An alternative mechanism must be considered in connection with posterior fossa tumours, namely obstruction of the right lateral sinus by a mass in its neighbourhood. Since this sinus usually forms a continuation of the superior longitudinal sinus, obstruction at this point may sufficiently impair the absorption of cerebro-spinal fluid to cause some degree of hydrocephalus; a mechanical disturbance that has been more fully discussed elsewhere (p. 86). In one case in this series (P.M. 242/1936) a meningioma riding the right lateral sinus was associated with an appreciable degree of hydrocephalus. There

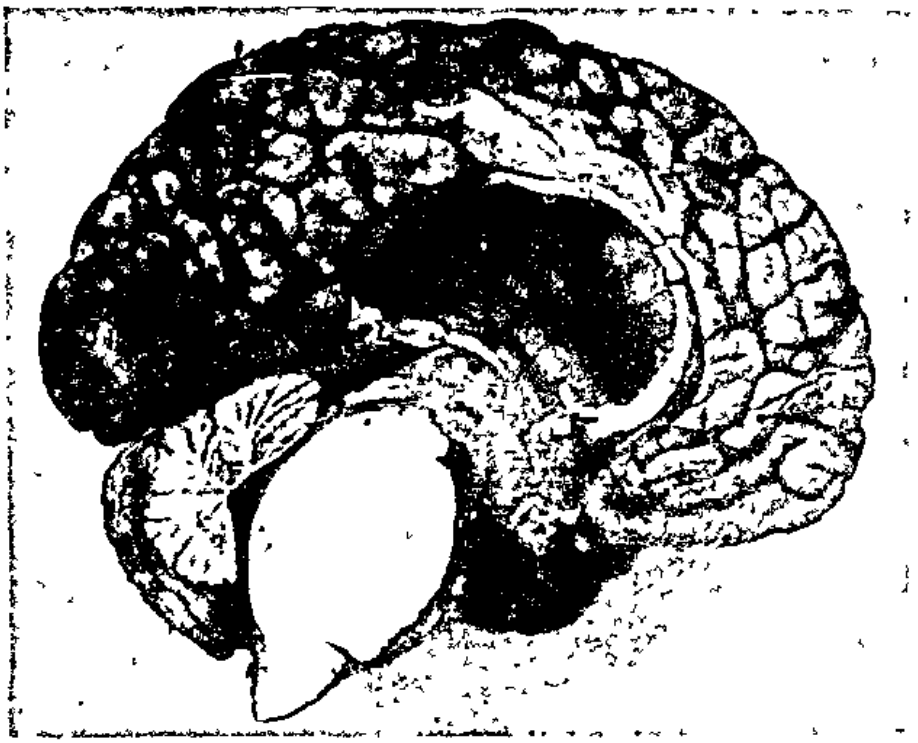


FIG 70: Diffuse astrocytoma of pons in mid-sagittal section (P.M. 240/1937). Note deformity of fourth ventricle. The mass in the floor of the third ventricle is a small suprasellar craniopharyngioma

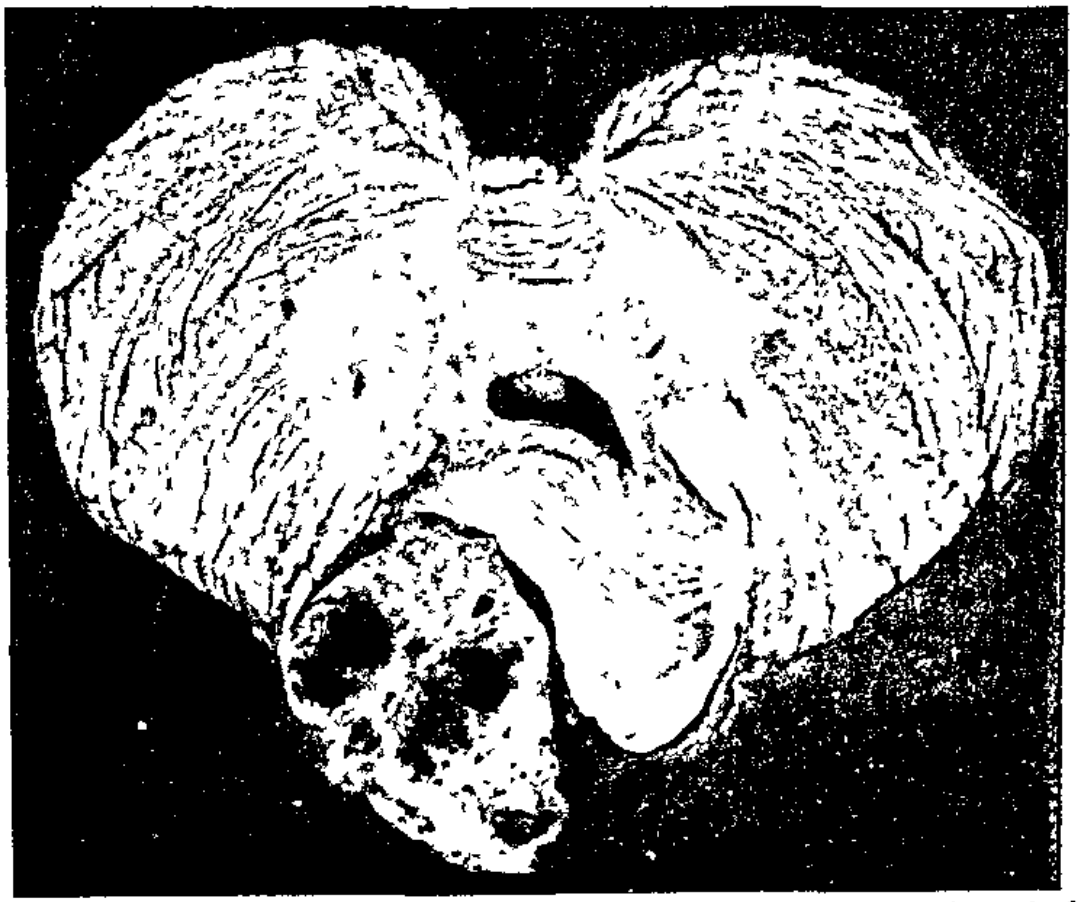


FIG. 71: Schwannoma of fifth nerve, showing deformation of pons and anterior end of fourth ventricle

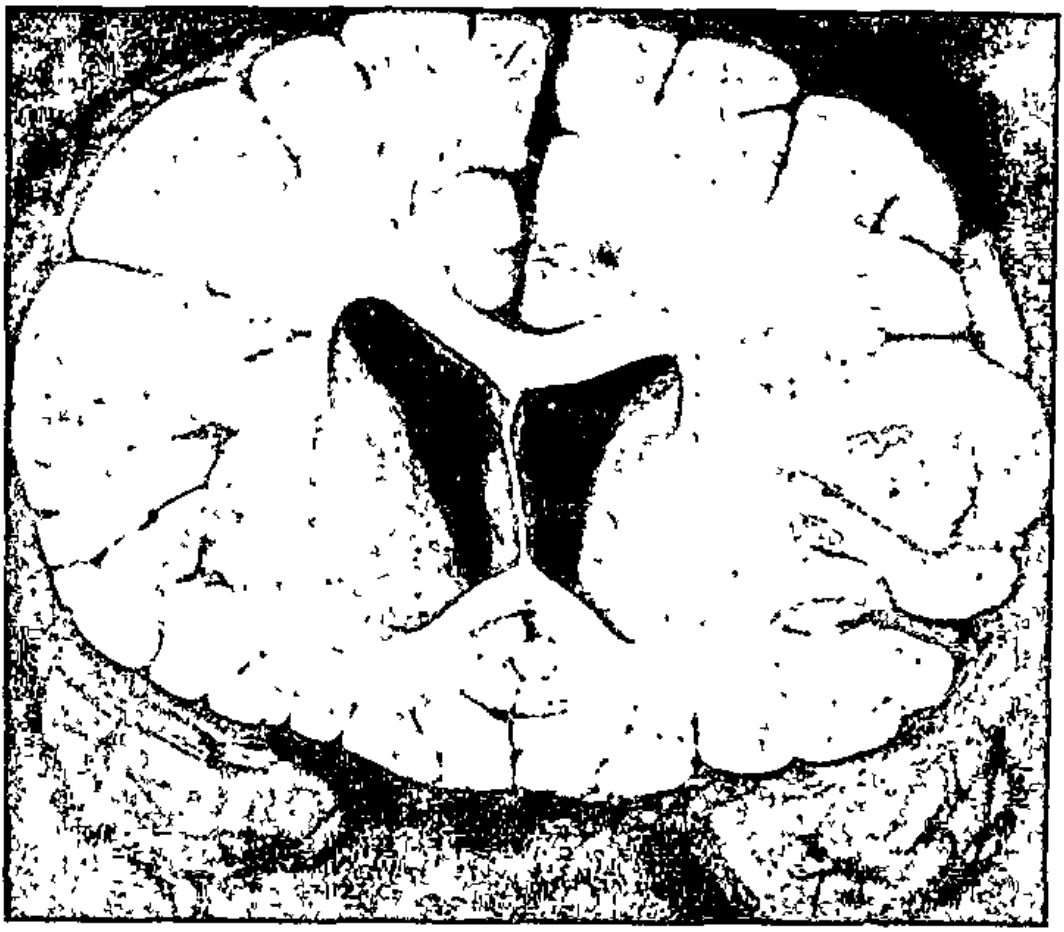


FIG 72 Coronal section through anterior horns showing the hydrocephalus associated with the tumour in Fig. 71

was, however, no actual occlusion of the lumen though it was considerably compressed, and it might alternatively be argued that the hydrocephalus in this case was due to interference with the circulation of the cerebro-spinal fluid in the basal cisterns.

Diffuse Tumours of the Leptomeninges

The consideration of these tumours might appropriately have been taken up in the section on meningitis because tumour cells in the leptomeninges stir up an inflammatory reaction, with the production of reticulin and fibrosis, of the same character as that excited by red corpuscles and foreign particulate matter. These diffuse tumours are almost invariably secondary, but there is one primary form which, though exceedingly rare, is of considerable interest, namely melanosis.

MELANOSIS

Diffuse melanosis of the leptomeninges was first described by Virchow (1859). It is a naevoid condition that is liable to affect the ventral aspect of the brain-stem, where melanin-containing cells ordinarily occur in the pia. In melanosis these cells acquire a neoplastic character and form a deeply pigmented layer throughout the basal cisterns and the adjacent cerebellum, as admirably shown in the case reported by Farnell and Globus (1931) in a boy of 16 (Fig. 73). In this example there was a cystic expansion of the cisterna magna, described as

being of the size of a base-ball, which was filled with a brownish, thick fluid. There was also a generalized distension of the ventricles which the authors attributed to the blockage of the pontine and interpeduncular cisterns. Such a condition would seem clearly to be of a developmental character especially as it is generally associated with pigmented moles, sometimes of great size, in the skin of other parts of the body. In their review of previously reported cases Schnitker and Ayer (1938) suggest that melanosis has not been recognized in infants. But the well-documented cases of Grahl (1906) and of Berblinger (1915) establish the occurrence of the condition at birth, and at 9 months respectively. To these may now be added the single example, in a stillborn hydrocephalic infant, occurring in the present series (P.M. 473/1931). Perforation of the head was necessary to effect delivery, and the excess of recent clot within the cranial cavity somewhat obscured the macroscopic appearances.

FIG. 73: Melanosis. Drawing to show the pigmentation of the leptomeninges at the base of the brain and the enlarged cisterna magna. (By kind permission of Dr. J. H. Globus)

The cisterna magna was greatly ballooned, as in the case of Farnell and Globus, and there was a diffuse café-au-lait pigmentation of the cerebellum and brain-stem, extending through the basal cisterns into the Sylvian fissures and involving the margins of the adjacent nervous tissues. A complete necropsy, including examination of the eye-balls, revealed no tumour elsewhere, but there were small pigmented naevi in the skin of the back, the right temple and submaxillary region. Microscopically the cells of these cutaneous naevi (Fig. 74) were

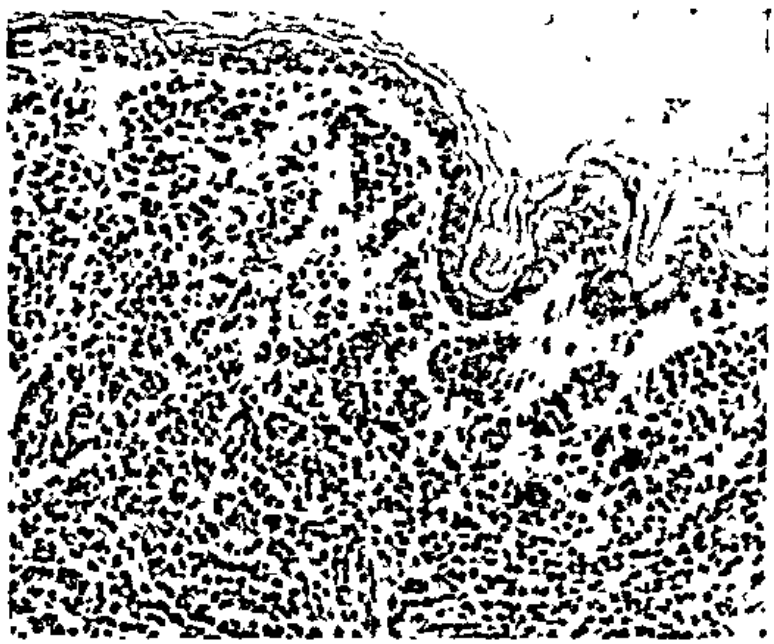


FIG. 74: Pigmented mole of skin of back in P.M. 473/1931. The cells are similar to those of the naevus in the leptomeninges. H. and E. × 170

FIG. 75: Melanosis (P.M 473/1931). Extension of the naevus cells along perivascular sheaths into cerebellum. H. and E. × 170

identical in appearance with those in the leptomeninges (Figs. 75 and 76) and contained large quantities of melanin. Not only did the cells diffusely occupy the leptomeninges but they extended for considerable distances into the brain-stem and cerebellum along the Virchow-Robin spaces of the perforating vessels, and sometimes invaded the adjacent nervous tissue (Fig. 75). Similar cells

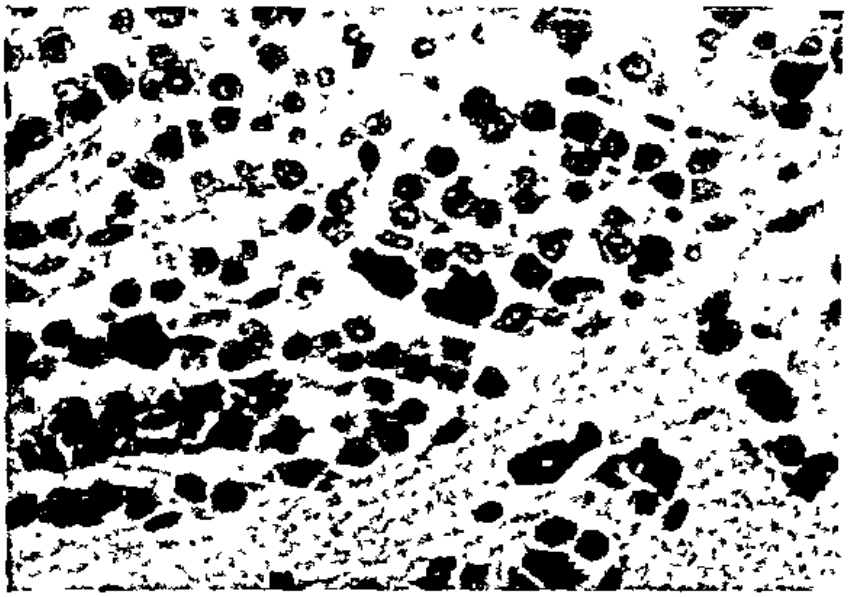


FIG. 76: As in Fig. 75, showing dark masses of melanin pigment within cells. Fontana. × 450

containing melanin pigment occupied the stroma of the choroid plexus of the fourth ventricle, but not of the lateral ventricles, and the inner layers of the dura at the foramen magnum. The effect produced upon the brain as a whole in this condition bears a close resemblance to that seen in any form of chronic meningitis, and ventricular dilatation is to be attributed to blockage of the cerebro-spinal pathway in the basal cisterns.

PRIMARY SARCOMATOSIS

Though the condition has been described in various publications no example occurs in the present series. Many of the older reports evidently confused the condition with gliomatosis of the meninges, especially that arising in association with medulloblastoma of the cerebellum. In other instances the head only was examined at necropsy, and the possibility that the tumour was in fact secondary cannot be excluded. In all doubtful cases the orbits should be included in the examination.

SECONDARY TUMOURS

The condition in which secondary carcinoma is widespread in the leptomeninges is well known under the name of meningitis carcinomatosa. Nevertheless it is rare and only four examples have been identified in the records of the London Hospital. Secondary sarcomatosis seems to be even rarer but, in a recent remarkable case (P.M. 254/1944), in a girl of 4 years, secondary rhabdomyosarcomatosis of the leptomeninges was found in conjunction with a primary rhabdomyosarcoma of the petrous bone. Internal hydrocephalus of a moderate degree was also present.

Gliomatosis of the leptomeninges is usually secondary to medulloblastoma, but may complicate spongioblastoma multiforme and various other types of glioma. A remarkable effect, macroscopically indistinguishable from post-meningitic hydrocephalus and of surprising chronicity may result from the diffuse spread of an oligodendroglioma abutting on the ventricular system or situated in the spinal cord. A group of such cases has already been published (Beck and Russell, 1942). Since then a further similar example has been reported (Blumenfeld and Gardner, 1945) and we have seen another since our first series was published which is sufficiently remarkable to merit a description here.

Case 51 F.W., a man aged 37 (R.I. 10698/1943) was admitted to the Nuffield Department of Surgery on June 7th, 1943, suffering from severe frontal headache, vomiting and bouts of giddiness which dated from a fall three months before admission. Deterioration of vision began three weeks after the accident At another hospital bilateral papilloedema was found, and lumbar puncture yielded slightly yellowish fluid at a pressure of 360 mm, containing 320 mg per cent. of protein and 2 lymphocytes per c mm. One month before admission there was slight weakness of the right hand and the right knee- and ankle-jerks were not elicited He suddenly became unconscious and a right subtemporal decompression was performed, from which he made a fair recovery.

On examination he was a left-handed man. The decompression was bulging and he showed some aphasia, relative anosmia, left facial weakness and paresis of the left arm, with weakness and ataxia of the left leg. The tongue was protruded to the left. Sensation and other neurological features were normal Lumbar puncture yielded fluid at 500 mm. pressure containing 1,000 mg. per cent. of protein and no increase of cells. After admission the decompression suddenly became slack and his condition improved. Ventriculography revealed symmetrical dilatation of the ventricles. He was discharged on June 29th, but readmitted a month later on account of recurrence of his symptoms and renewed bulging at the site of decompression. Examination showed deterioration in respect of the earlier clinical abnormalities, added to which he now showed gross motor aphasia and marked impairment of postural sense on the left side and impaired appreciation of cotton wool and pinprick in the left arm. The tendon reflexes were increased on the left, and the left big toe gave an extensor plantar response The cerebro-spinal fluid was unaltered in character. Ventriculography showed an increase of the ventricular dilatation. He died suddenly before a further operation could be performed

Necropsy: (R.I. P M. 419/1943): *Internal hydrocephalus: Gliomatosis of the leptomeninges. Intramedullary glioma of the cervical cord.* No significant changes were found in the other organs.

Examination of the brain and spinal cord The leptomeninges over the base of the cerebellum, and to a less extent in the cisterna basalis and over the adjacent temporal lobes, showed a diffuse greyish-white infiltration. A mass (1 cm. in diameter and 0 3 cm thick) of firm white growth occupied the arachnoid over the diaphragma sellae, displacing the pituitary stalk posteriorly and cupping the superior surface of the pituitary body. The meninges over the cerebral convexities appeared normal The hernia cerebri (9 by 7 by 4 cm) in the right temporal region contained a traumatic cyst in the subcortical white matter which reached the ependyma of the temporal horn but did not communicate with the ventricle. The ventricles were moderately dilated. Miliary and smaller nodules of growth occupied the ependyma of the fourth ventricle, and a few were present in the third The ependyma elsewhere was normal.

In the spinal cord there was great irregular infiltration, up to 0·4 cm thick, of the pia-arachnoid over the posterior surface with similar grey, gelatinous growth. It was greatest over the thoracic segments. A nodule of growth, 0 5 cm in diameter, occupied the tip of the filum terminale. On section a circumscribed, soft greyish-white, and in places haemorrhagic, tumour expanded the cord from the third cervical to the first thoracic segments. Its greatest diameter, 1·2 by 0 5 cm, was in the seventh cervical segment and it reached the posterior surface of the cord in the third, fourth and fifth segments, and the anterior surface in the first thoracic segment.

Microscopic examination: The primary tumour and its meningeal extensions show the characteristic appearances of an oligodendroglioma, and many of the cells were specifically impregnated with silver in frozen sections of the primary mass. As in the cases already reported there is a considerable diffuse chronic inflammatory reaction with fibrosis in those parts of the meninges that are occupied by tumour cells.

In this case the symptoms were due mainly to the extension of the tumour in the meninges, with resulting hydrocephalus. The presence of an intra-medullary tumour of the spinal cord was not suspected clinically. An

interesting demonstration is thus afforded of the retrograde spread of cells in the cerebro-spinal pathway, both through the meninges and also to the ventricular cavity. The oligodendrogliomata appear to be exceptional in the long survival of subjects who show this diffuse meningeal spread. In the present instance the history was short but, in our published series (Beck and Russell, 1942), Case 1 was certainly affected for a period of seven years and, in the more recent case of Blumenfeld and Gardner, the history dated to fourteen years before death. In such cases the clinical and macroscopic features are more suggestive of a chronic arachnoiditis than of tumour and, indeed, the primary tumour may be so small as to evade clinical localization.

Diffuse tumours of the leptomeninges may thus simulate chronic meningitis and may likewise cause internal hydrocephalus. It has already been seen that circumscribed meningeal tumours of the posterior fossa, particularly those of the cerebello-pontine angle, also produce hydrocephalus and the possible mechanism here has been briefly discussed. It might be thought likely that similar tumours situated at or near the base of the brain above the tentorium would, by interfering with the passage of cerebro-spinal fluid from the basal cisterns to the convexities, also be productive of hydrocephalus. Thus Cairns (1939) in his account of the operative removal of a sphenoidal-ridge meningioma, describes the gush of cerebro-spinal fluid with consequent relief of intracranial tension that takes place as soon as the main body of the tumour is levered out of its bed in the Sylvian fissure; and he regards this as a characteristic phase of the operation (personal communication). Examination of the brain in seven cases of meningioma of this region, together with three cases of olfactory-groove meningioma and three cases of meningioma of the cavernous sinus and suprasellar region has however, provided no clear evidence of an associated hydrocephalus. In four instances out of thirteen some degree of ventricular dilatation was, indeed, noted, but inflammatory processes in these cases could not be ruled out.

CHAPTER VII

ANATOMICAL EFFECTS OF HYDROCEPHALUS

AN outline of the pathological alterations in anatomical structures resulting from internal hydrocephalus forms the concluding section of the present study. These alterations are divisible first into certain general effects upon the body as a whole, and secondly, into the more strictly local effects upon the skull and its contents.

General Effects

In certain slowly progressive cases of internal hydrocephalus in adolescents the *Fröhlich syndrome* may make its appearance. This is attributable to pressure upon the infundibulum, and is associated anatomically with great ballooning of the floor of the third ventricle which is closely apposed to the deeply-cupped surface of the diaphragma sellae. Erosion of the posterior clinoid processes and the outward expansion of the walls of the sella turcica may present radiographic appearances which, in combination with Fröhlich habitus, tempt the clinician to consider the diagnosis of pituitary tumour (see Case 26, p. 44). The extraordinary rarity of such tumours in adolescence should, however, season judgment. Instances of this type of disorder have been exemplified in association with tumours of the mid-brain (Cases 49 and 50, pp. 100 and 102). The Fröhlich syndrome may also accompany slowly growing subtentorial tumours such as capillary haemangeioblastomata and astrocytomata, when hydrocephalus is great (Fig. 77). Yet it is difficult to understand how it comes about that, in other cases of similar type, where the ballooning of the third ventricle is equally great, the Fröhlich syndrome does not develop.

FIG. 77: Haemangeioblastoma of medulla oblongata occluding hind end of fourth ventricle. Fröhlich's syndrome was present (P.M. 449/1930)

A detailed analysis of the possible histological changes in the hypothalamic centres, and their comparison in the different cases, might supply the answer to this problem.

A rarer bodily effect, not seen in the present series apart from tumours of the pineal and hypothalamus, but reported by several authors, is that of *precocious puberty* in cases of internal hydrocephalus. Bournville and Noir (1900) reported a case of precocious puberty in a girl of 9 years in whom hydrocephalus followed convulsions at the age of 6 months. Menstruation began at the age of 9 years. The photograph illustrating their paper shows the child supported by a nurse: there is marked development of the breasts and pubic hair. At necropsy complete obliteration of the aqueduct was observed macroscopically but the histology is not described. Dorff and Shapiro (1937) record the case of a girl aged 6½ years who had suffered from meningitis at the age of 2 months. The family physician and a paediatrician confirmed that she had then been acutely ill with fever and convulsions which lasted for a week. Following that, according to the mother, there was both blindness and rigidity of the legs for three months. She then recovered and, at the age of 5, developed a general plumpness, enlargement of the breasts, growth of axillary and pubic hair, and a mature voice. On examination the head measured 64·5 cm. in circumference. She was mentally dull. Vision was "fair, but definitely impaired". The external genitalia were of mature type. Death followed ventriculography, and necropsy revealed gross internal hydrocephalus which was due to chronic basal meningitis. The pituitary gland was somewhat enlarged and compressed, but was of normal structure. The third ventricle showed chronic ependymitis. Lhermitte (1938) reported a somewhat similar case in a boy who developed internal hydrocephalus following injury to the skull at the age of 8 years and showed marked development of the genitalia at the age of 10, described as being equivalent to that usually seen at the age of 16 or 17 years. At the same time a slight down appeared on the upper lip, he rapidly increased in height and his voice became rough. At the time of writing the boy was still alive. A less pronounced example has also been briefly described by Schlesinger (1934) in a girl of 8 years who suffered from an attack of meningitis at the age of 4 months.

In seeking an explanation of this development of precocious puberty in association with internal hydrocephalus it is necessary to take stock briefly of the incidence of this bodily abnormality in conjunction with intracranial disease in general. Until recently tumours of the pineal body have been the only intracranial abnormality commonly recognized in precocious puberty, and a disturbance of the hypothetical internal secretion of the pineal has been postulated as the explanation of premature sexual development. Some would perhaps argue that Lhermitte's case was of this nature, setting aside the history of trauma as unessential. And support might be found for this view because Lhermitte admits that "convulsive crises" occurred in early childhood and that there was, at this earlier stage, retardation of both physical and mental development. The child was therefore abnormal before the time of the injury. In recent years, however, various cases have been reported in which precocious puberty has been associated with a hypothalamic tumour, the pineal being normal. These tumours are usually astrocytomata, and are apt to be massive, thus obstructing the cavity of the third ventricle and giving rise to secondary hydrocephalus. More instructive are the rare cases of hypothalamic tumour with precocious puberty in which hydrocephalus is absent. In the report of an

example of this kind (Le Marquand and Russell, 1934-35) Le Marquand argued that the precocious puberty should be regarded as the effect of some abnormal stimulation of the hypothalamic centre regulating the secretion of gonadotropic hormones. The theory is discussed and endorsed by Gross (1940) in his report of a similar case, and by Poston and Barber (1942) who observed gross genital hypertrophy in a boy of 1 to 2 years who had a small astrocytoma, about the size of a walnut, attached to the left corpus mammillare. If this view is accepted, and there seems no reasonable argument against it, then it must also be accepted that a similar stimulus may be set up in some cases of hydrocephalus where no tumour is present, as in the instructive case of Dorff and Shapiro. In conformity with this, the complication of some pineal tumours by precocious puberty may also be explained by the presence here also of internal hydrocephalus for, as already mentioned, these tumours press upon the quadrigeminal plate and obliterate the aqueduct. The emphasis is thus shifted from the tumour to its secondary effects and it becomes rather easier to understand why precocious puberty may be associated with a variety of histological types of pineal tumour, and why no one type is consistently complicated in this way.

Kraus (1933) has claimed that the pituitary gland in cases of increased intracranial pressure, when assayed biologically by the effect on immature mice, showed a 60 per cent. increase of follicle-stimulating factor in females. He considered it necessary that there should be no destruction of the hypothalamus, hypophysis or infundibulum though the walls of the third ventricle might be thinned from pressure. Equivocal results were, however, obtained by Henderson and Rowlands (1938) in an assay of 109 human pituitary glands from 57 subjects (28 male and 29 non-pregnant females) with normal intracranial pressure, and from 52 subjects (28 male and 24 non-pregnant females) with cerebral tumours and increased intracranial pressure. In the controls they found that the gonadotropic activity varied with age, increasing to the end of the peroid of sexual activity and showing a sudden rise in the female at the menopause. With increased intracranial pressure the hormone tended to be more variable than in normal subjects. But several of the women showed menstrual dysfunction and in these there was a suggestion of a premature rise in the amount of gonadotropic hormone in their pituitaries.

If the pituitary can be over-stimulated by pressure upon the floor of the third ventricle it might be expected that other manifestations of excessive activity such as *acromegaly* would be observed. But the only instance of this in hydrocephalus that I have found in the literature was Cushing's Case 38 (1912). This was in a man of 33 who, during the year before operation, had developed acromegalic features, unsteadiness on his feet, and vertigo. At operation the pituitary stalk was accidentally divided and he died three days later from cachexia hypophyseopriva. At necropsy a large cerebellar cyst was disclosed, and a moderate hydrocephalus. The suprarenals and thyroid gland were enlarged, as were the islets in the pancreas. Unfortunately the complete degeneration of the anterior lobe of the pituitary gland made its staining ineffective. The final word therefore could not be said, but Cushing's opinion was as follows: "Whether the hypophyseal hyperplasia was merely a concomitant process which bore no relation to the obstructive hydrocephalus, or whether the gland had been aroused into its state of pathological overactivity as a secondary result of the cerebellar lesion, cannot be positively certified. I incline towards the latter view."

In some cases of internal hydrocephalus growth appears to be retarded and frank *infantilism* may even be observed, as in the remarkable case of Touche (1902). He described a woman of 29 with the stature of a child of from 6 to 7 years though her head was of adult size. Her history was one of normal development up to the age of 4 years when she suffered from convulsive attacks followed by coma over a period of four months. This was succeeded by complete paralysis of both sides of the body, gradual increase in the size of the head and complete arrest of growth. Partial power of movement returned later to the upper limbs. At necropsy there was great internal hydrocephalus due to obliteration of the aqueduct at a level between the anterior and posterior corpora quadrigemina. The microscopical appearances of this lesion were not given.

Briefly, therefore, a variety of hypothalamic disturbances can accompany internal hydrocephalus but, in general, they appear to be restricted to childhood and adolescence and affect relatively few cases.

Local Effects

The alterations in the structure of the *skull* are known to all and are well described by West (1848) as follows: "Few objects are more pitiable than a little child who is the subject of far advanced chronic hydrocephalus. While the skin hangs in wrinkles on its attenuated limbs, the enlarged head appears full, almost to bursting, owing to the stretching of the scalp, and the scanty growth of hair does not at all conceal the distended veins that run over its whole surface. The size of the skull, too, appears greater than it really is, since the face not only does not partake of the enlargement, but retains its infantile dimensions much longer than natural. The eyes are so displaced by the altered direction of the orbitar (*sic*) plates, that the white sclerotic projects below the upper lid, and the iris is more than half hidden beneath the lower."

In longstanding cases of hydrocephalus it may be found that accessory bones arise in the dura of the vault : the so-called *ossa triquetra* or Wormian bones. These were well described and illustrated by Richard Bright (1831) in his account of the famous case of James Cardinal (Vol. 2 of his Reports of Medical Cases). This case was in a young man of 29 who had been hydrocephalic from birth but whose head had undergone little change in size from the age of 5 years. The bones of his skull did not finally close till he was 27, the anterior fontanelle being ossified last. The capacity of his skull was altogether 10 pints. On examination at necropsy the dura mater showed extensive deposits of bony matter in thin plates, some of which were almost of the thickness of a shilling.

While this ossified condition of the dura is but rarely seen in hydrocephalus, a stage, which may well be a precursor, in which the membrane is speckled with opaque white flecks of amorphous chalky material, is quite common in children suffering any long sustained rise in intracranial pressure. Histologically (Fig. 78) this appearance is due to the deposition of fine particles of calcium in the dura, preceded and accompanied by degeneration of the collagen fibres and necrosis of the cells throughout the area. The deposition of bone at later stages is not surprising when it is recalled that the dura is no more than a specialized form of periosteum.

When the sutures have already been closed the ability of the skull to expand is very limited. But the inner table usually shows shallow excavations, the so-called digital impressions or convolutional markings, from the pressure

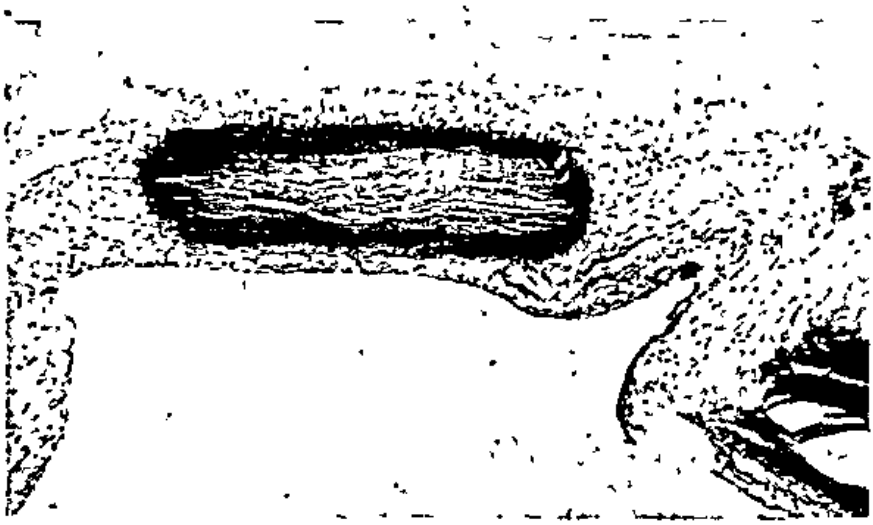


FIG. 78: Dura from cerebral convexity in a girl of 6 years with a cerebral glioma, showing calcified area in the collagen. H. and E. × 50

exerted upon it by the cerebral convolutions. This well known X-ray appearance is characteristic of increased intracranial pressure. It seems remarkable that so soft a tissue as that of the brain should be able to deform ivory bone, and doubtless much of the alteration seen in the inner table is the result of re-modelling of the bony architecture. The process is more obvious at the base where the cribriform plates are deeply sunken in a bowl-like depression of the anterior fossa. Erosion of the posterior clinoid processes has already received mention (p. 114); in addition it is not uncommon to find smooth-walled excavations varying in size and resembling pot-holes in the middle fossae.

FIG. 79: Part of base of skull in a case of cerebral astrocytoma, showing erosion of bone of left middle fossa, dorsum sellae and orbital plate

Those shown in Fig 79 are exceptionally large. These hollows are occupied by protrusions of the cerebral cortex through the meninges, the dura in this region normally being somewhat thin and fenestrated. The cortical tissue does not, however, come into direct contact with the bone. When the dura is reflected from the middle fossa the small bosses of tissue occupying the excavations separate cleanly from the bone and give the appearance of nodules of growth upon the exterior surface of the membrane. On microscopical examination the core of a nodule is composed of cortical tissue, in which the pyramidal cells are often surprisingly well preserved, enclosed by dense fibrous tissue derived from the blended lepto- and dural-meninges. Fig. 79 also shows erosion of the clinoid processes, and the lesser wing of the sphenoid, a pear-shaped deficit in the orbital plate exposing the underlying adipose tissue, and also the marked concavity of the whole region of the tuberculum sellae and cribriform plates. The bone here was so thin that a hole was accidentally made with the point of the forceps at the hinder part of the left cribriform plate during the stripping of the dura.

When one considers the effect on the *brain* itself, it is invariable that the ventricular dilatation and consequent thinning of the cerebral substance do not affect all parts equally. The thinning is usually greatest over the convexities and especially the frontal and temporal poles. The basal ganglia are usually surprisingly free from deformation. The foramina of Monro are enlarged and the intercerebral commissures elongated. In almost all cases where hydrocephalus is advanced the septum pellucidum becomes fenestrated (Fig. 63 p. 102) and may be reduced to a mere fringe in the grosser expansions of infancy. The cavum of the septum is often widely dilated in instances where the septum itself is intact. The corpus callosum is apt to be greatly thinned. Characteristic deformations of the walls of the third ventricle are seen in the ballooning of the floor, as already mentioned, the supra-optic recess and the supra-pineal recess. The cavity of this ventricle is thus greatly elongated in the mid-sagittal plane as well as in the vertical plane. The *choroid plexuses*, especially in the lateral ventricles, are generally more or less atrophied ; this has been advanced as an argument in favour of the theory that they are responsible for absorption of the cerebro-spinal fluid. But, as demonstrated by Flexner (1933), the secretory activity of the choroid plexuses is inversely proportional to the level of the ventricular pressure. With a rising pressure, therefore, a gradual cessation of activity may explain some part of the atrophy. In the absence of inflammation microscopical examination does not reveal any remarkable histological alterations in structure.

Certain histological changes are to be noted in the *ependyma* and *subependymal tissues*. It is not generally recognized that in advanced hydrocephalus the ependyma is often destroyed over wide areas without any obvious alteration of the macroscopic appearances. As a result the subependymal glia comes to line the ventricle in these parts. Consequently many experiments which purport to show that the absorption of cerebro-spinal fluid may take place through the ependyma are valueless because the establishment of internal hydrocephalus has played an intrinsic part in such experiments.

In chronic inflammatory conditions the ependyma is often studded with minute granulations, a condition often referred to as granular ependymitis. It was formerly thought to be especially associated with syphilis, and is indeed a frequent but not invariable feature of the brain in general paralysis. But the investigation of any large series, such as the present, clearly shows that this condition of the ependyma is non-specific: it may accompany any type of

chronic inflammation, and is perhaps best seen in such (as in Fig. 80), but may also be found in association with a variety of cerebral tumours including sub-tentorial examples, and with congenital malformations, for example true stenosis of the aqueduct (Case 2, p. 13 which, it will be noted, was in a stillborn infant). These associations suggest that the true basis of granular ependymitis is mechanical rather than inflammatory. Microscopical study of the ependyma in a wide range of pathological conditions indicates that the

FIG. 80: Granular ependymitis over basal ganglia from a case of hydrocephalus secondary to chronic meningitis. Phosphotungstic-acid haematoxylin. × 23

ependymal cells are both highly susceptible to injury and have little or no regenerative capacity. In spite of repeated search mitotic figures have never been identified in these cells. The sub-ependymal glia on the other hand being composed, for the most part, of fibrillary astrocytes, has considerable powers of proliferation. The preliminary step in the formation of a granulation is the denudation of the superficial ependymal cells. This, as already pointed out, is a common feature in hydrocephalus whether granulations are present or not. Stages in the proliferation of the exposed subependymal glia can then be traced from a slight heaping-up of the cells above the level of the adjacent surface, to the polypous masses shown in Fig. 80. Neighbouring granulations may, and often do, fuse with one another to form plateaux of glia beneath which isolated remnants of ependyma can be identified in characteristic rosette-formations. Some stimulus is doubtless required to bring about this glial proliferation: about this nothing is known, but the relative frequency of granular ependymitis in cases showing evidence of an earlier leptomeningitis suggests that inflammation has played some part, though the absence of any inflammatory cellular infiltration in the neighbourhood of the granulations denies corroborative evidence.

A distinction must be made between this true granular ependymitis and "ependymitis blastomatosa", a rarer condition in which secondary deposits of new growth arise in the ependyma following the dissemination of tumour cells in the cerebro-spinal fluid. The primary tumours with which this is most commonly associated are medulloblastoma and spongioblastoma multiforme; oligodendrogliomata that abut on the ventricular system may also metastasize in this manner (Beck and Russell, 1942). The tumour-like texture of the

nodules, their greater variability in size and, finally, microscopical examination make the distinction from granular ependymitis easy.

Collagenous replacement may arise as a focal change in the ependyma in cases of internal hydrocephalus of the post-meningitic type. This is recognizable with the naked eye as well-defined white patches suggestive of

FIG. 81: Same case as in Fig. 80 showing replacement of ependyma by collagen in occipital horn. H. and E. × 20

leukoplakia as seen, for example, in the oesophagus. Under the microscope (Fig. 81) the collagenous fibres lie longitudinally upon the surface of the subependymal glia, and at certain points dip into the glia to unite with the walls of the adjacent vessels, which also show collagenous thickening. In the example illustrated there was no trace of cellular inflammatory infiltration, but there can be little doubt that the change was due to an antecedent ependymitis at the time of the active meningitis. Granular ependymitis was pronounced in the same case.

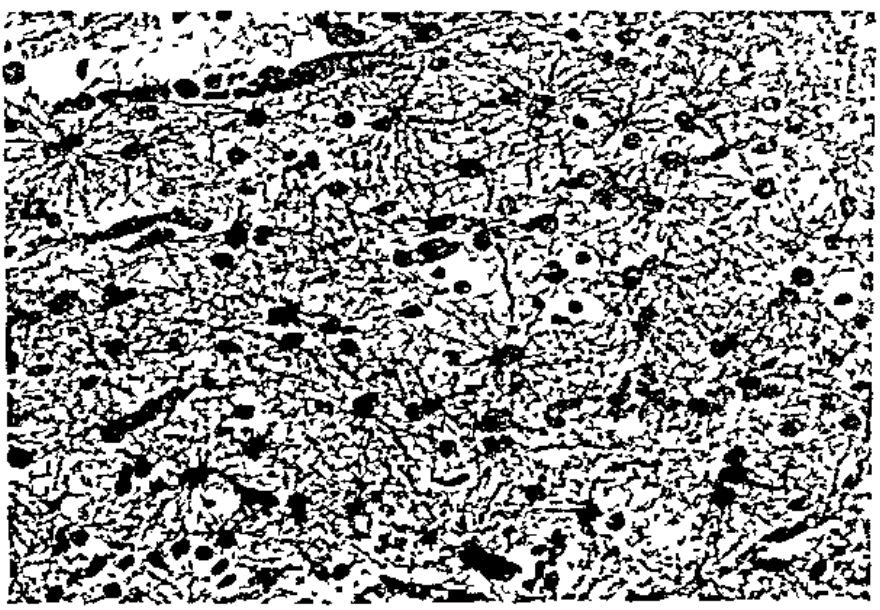


FIG. 82: *Case 2:* Subependymal gliosis in lateral ventricle from a stillborn infant with stenosis of the aqueduct. Silver carbonate method for astrocytes. × 230

The subependymal glia usually undergoes a variable degree of gliosis in association with internal hydrocephalus, and this may be quite pronounced in infancy, as shown in Fig. 82, taken from the brain of a stillborn infant in which perforation of the head was required to effect delivery. The hydrocephalus was due to stenosis of the aqueduct.

This gliosis presumably arises as a reaction to pressure just as the marginal, or sub-pial, neuroglia increases in density over the cerebral convexities when there is a prolonged increase of intracranial pressure. A similar reaction of the marginal glia accompanies chronic leptomeningitis. By analogy subependymal gliosis is presumably likewise promoted by chronic ependymitis. In its nature such gliosis tends to counteract the pressure of the fluid from within the ventricles, and the felting of the fibres ensures the uniformity with which expansion takes place in most instances. But specimens are encountered, in association with gross degrees of internal hydrocephalus, where the ventricular wall is focally ballooned in such a way that the ependyma actually reaches the surface of the brain over a considerable area, and comes into close apposition with the leptomeninges. The surface of the brain in such places presents a cystic, translucent appearance and when, as is frequent, the calcarine region is involved, there may be a considerable protrusion of the membranes. Doubtless this appearance has often been interpreted as due simply to extreme thinning of the brain substance. But histologically the mechanism, in those cases that have been examined microscopically in the present series, has proved to be a

FIG 83. Margin of translucent area in Rolandic region. Ventricle below and to left; the ependyma and subependymal glia (well-defined dark zone) come into apposition with the meninges. H. and E. × 10

herniation of the ependyma together with the subependymal glia through one of the deeper sulci of the cerebrum with wide separation of the bordering convolutions. The two sites of election in the brain are the calcarine and Rolandic fissures, particularly the former. Fig. 83 is a low-power photograph of the margin of such an area in the Rolandic region taken from a case of

astrocytoma of the mid-brain (see p. 98 ; Fig. 61). The ependyma and subependymal glia form a distinct layer skirting the border of the convolution and blending with the leptomeninges at the surface. Fig. 84, taken from the calcarine region in Case 2 (p. 13), shows at higher magnification the blending of the leptomeninges (above) with the ependyma and subependymal glia (below). A short strip of ciliated ependymal epithelium can be recognized towards the centre of the lower border. Though proof is of course lacking, it may be that this juxtaposition of the ependyma and meninges provides a means whereby the ventricular fluid can seep out into the subarachnoid spaces and thus be short-circuited. The great oedema of the meninges, seen in Fig. 84, supports this view.

FIG. 84: From translucent area in calcarine region in *Case 2*. Ependyma and subependymal glia are overlaid by oedematous leptomeninges. H. and E. × 113

Rupture of the ventricular wall with the formation of *false diverticula* is not uncommon, and may take place at one or more points in the lateral ventricles. A small orifice or slit in the lining of the ventricle then leads into a smooth-walled cavity filled with clear fluid. Such cavities, as illustrated in Fig. 85, taken from a case of tuberculous meningitis, are often small. Less frequently the diverticulum develops to a large size in the centrum semiovale and, by dissection of the white matter, forms an outer sac between the ventricle and the subcortical white matter. Two such cases have been reported (Northfield and Russell, 1939) in which the motor fibres were interrupted by the development of the diverticulum with consequent hemiplegia. Ventriculography, performed in one of these cases, provided a confusing picture owing to the entry of air into the diverticulum, and the nature of the abnormality was not

FIG. 85 Coronal section through frontal horns in a case of tuberculous meningitis showing a small false diverticulum in inferior angle of left horn

clarified until the necropsy was performed. This revealed a large diverticulum in the right hemisphere (Figs. 86 and 87) which communicated with the ventricle by a slit in the posterior frontal region and a second over the tip of the temporal horn. The clinical development of hemiplegia about six months before death agreed histologically with the advanced degeneration of the corresponding pyramidal tract (Fig. 88) For fuller details the reader is referred to the original article.

Rupture of the ventricular wall, occurring at points where the cerebral substance is greatly thinned, may permit the escape of cerebro-spinal fluid into the subarachnoid space, thus providing a short-circuit for the fluid: an arrangement that may be of great potential value to the patient if the aperture is suitably placed. This, which may be regarded as "nature's cure", is imitated by surgeons in the operation of ventriculostomy, whereby an opening is made into the anterior wall of the third ventricle thus permitting the fluid to escape into the cisterna chiasmaticus. What may be termed "spontaneous ventriculostomy" was described by de Lange (1929) in an infant who, having developed signs of internal hydrocephalus shortly after birth, survived for nearly two years and was found at necropsy to be suffering from an occlusive ependymitis of the aqueduct. In both frontal lobes a fistula was present permitting the exit of cerebro-spinal fluid into the leptomeninges, and it was considered by de Lange that this circumstance had enabled the infant to survive for so long. But the site at which such communications seem most apt to be formed is in the hinder part of the floor of the body of the lateral ventricles, where a thin lamina of white matter lying between the fornix and the forceps

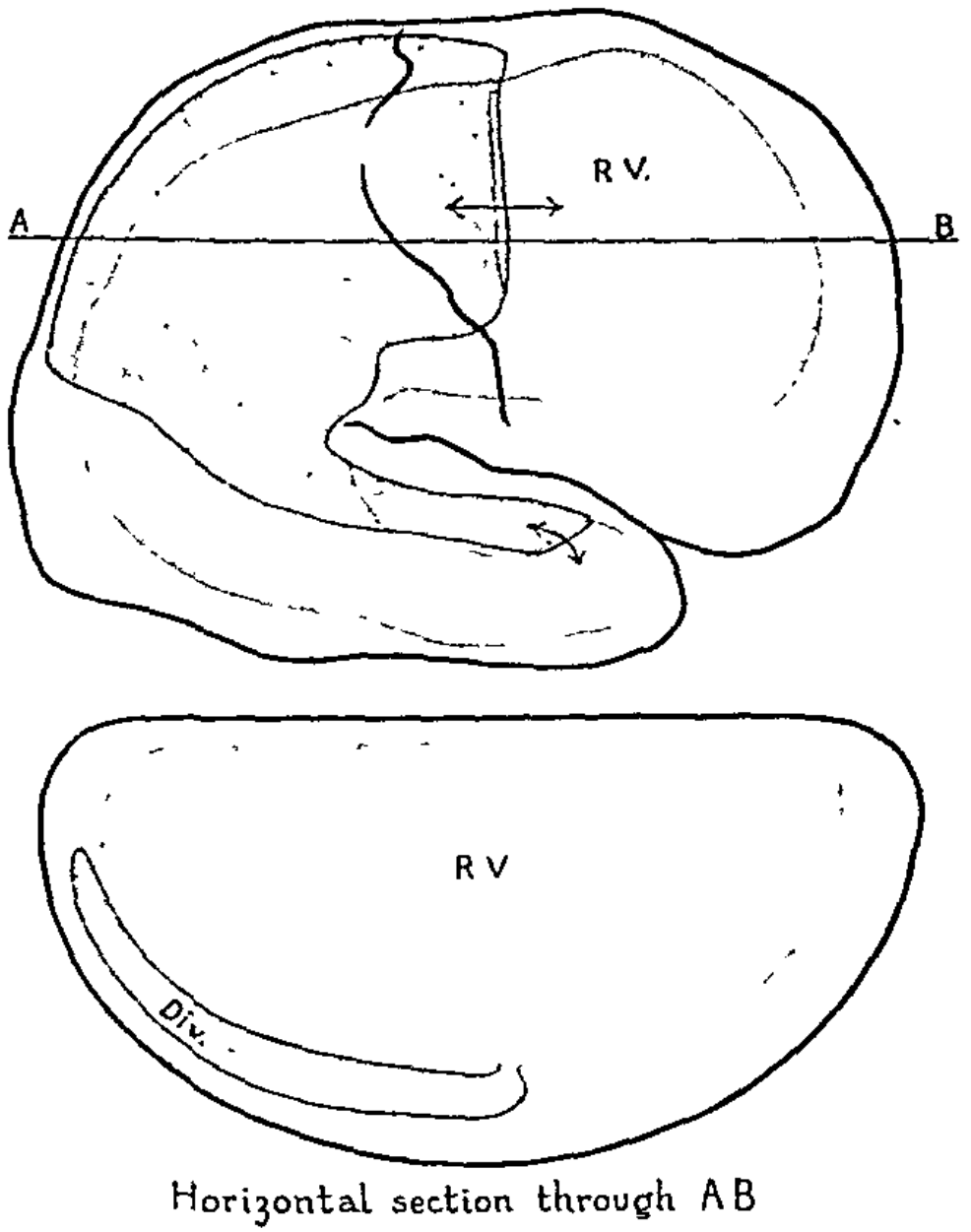


FIG. 86: Diagrammatic representation of relations of false diverticulum (darker area) to right lateral ventricle in Case 1 of Northfield and Russell (1939). (By kind permission of the Editor of *Brain*)

FIG. 87: Coronal section of cerebrum in Case 1 of Northfield and Russell (1939) showing false diverticulum on right

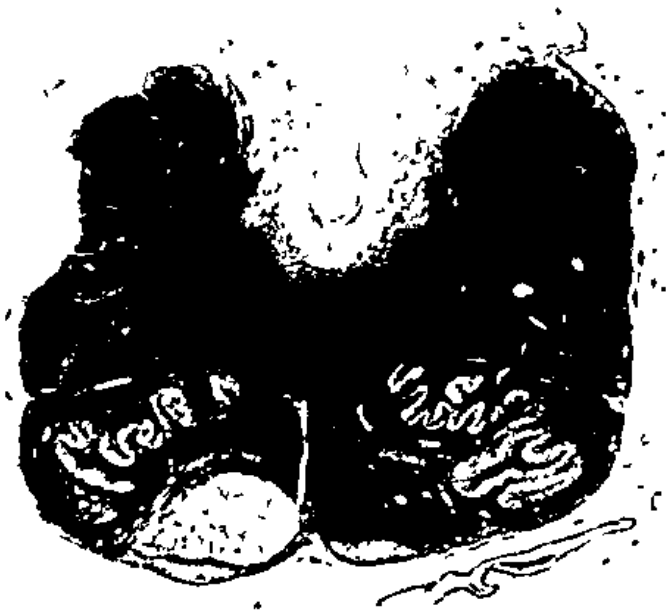


FIG. 88: Same case as in Fig 87 showing advanced degeneration of right medullary pyramid. Loyez' haematoxylin × 4 8

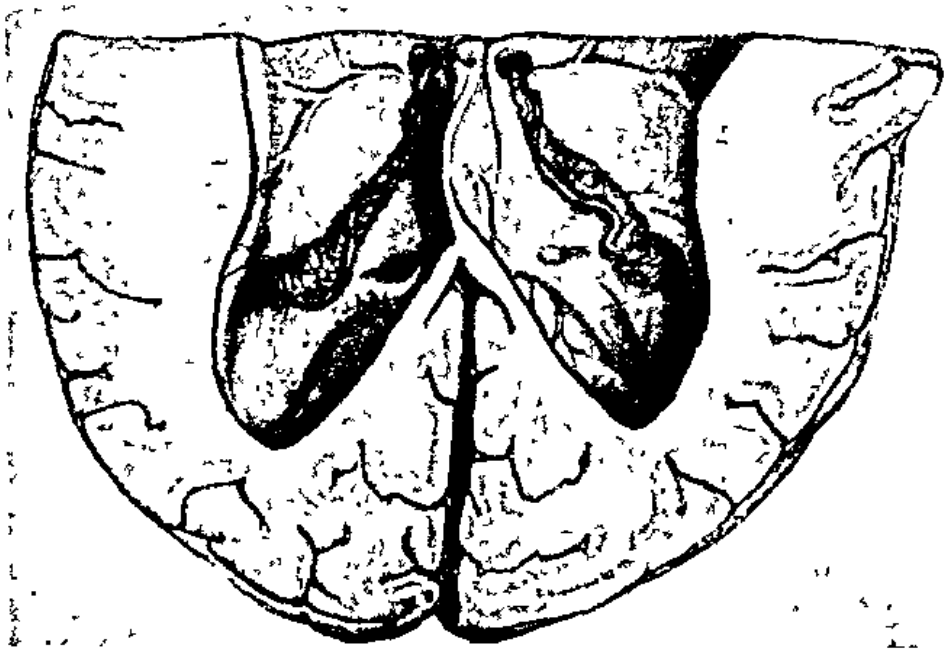


FIG. 89: Sketch of horizontal section of ventricles in Case 1 of Pennybacker and Russell (1943) showing spontaneous ventriculostomy on left and dimple at corresponding site on right

FIG. 90: Same case as in Fig. 89 showing relationship of opening to the meninges of the mid-brain. (By kind permission of the Editor, *Journal of Neurology, Neurosurgery and Psychiatry*)

major separates the hippocampal gyrus from the pineal body (Figs. 89 and 90). Cases in which this form of spontaneous ventriculostomy has occurred have been described by Sweet (1940), Childe and McNaughton (1942), and Pennybacker and Russell (1943). Stages preceding rupture, in which this area becomes dimpled or markedly translucent, have been observed (see the last reference). In retrospect it was found that an example of this form of communication between the lateral ventricle and the leptomeninges had been noted and entered in the records of the Bernhard Baron Institute by Professor H. M. Turnbull as early as 1923 (Case 24, p. 41). His description leaves little

room for doubt as to the character of the "cyst" found in the subarachnoid space over the dorsal aspect of the cerebellum. The passage of cerebro-spinal fluid under tension from the lateral ventricle into that part of the cisterna ambiens which lies over the quadrigeminal plate creates a cyst-like space which, in ventriculography, appears to be a diverticulum of the third ventricle. It may force its way through the incisura of the tentorium to overlap the cerebellum. In the absence of adhesions in the adjacent meninges the establishment of this spontaneous ventriculostomy may well prolong life, as the history in Case 24 seems to suggest.

The cerebro-spinal fluid, however, may break through the leptomeninges in ventricular rupture and enter the subdural space. The event is unfavourable to the patient because absorption of the fluid does not take place to any appreciable degree in this situation. This complication is all too apt to occur when surgical attempts to relieve hydrocephalus have involved opening the lateral ventricle, and may even occur after repeated puncture of the ventricles through the anterior fontanelle. Spontaneous rupture of this kind may take place through the corpus callosum, as in Bright's case, James Cardinal, previously quoted on p. 117. Bright records that, on opening the skull, the whole of the upper part of the cranium was filled with clear transparent fluid contained only within the dura mater. "The brain itself occupied the base of the cranium, the parts being so displaced that it was no easy matter to recognize all their bearings. An opening on one side of the corpus callosum permitted escape of fluid dorsalwards laying the two hemispheres outwards like the leaves of a book."

Finally, cases are recorded in which spontaneous *rupture of the head* has occurred in hydrocephalus, and the cerebro-spinal fluid has spouted forth in an unpleasantly dramatic fashion (Amyot, 1869). Fortunately this seems to be a rare event of the past, and would probably be forestalled by relieving surgical measures at the present time. A more beneficent arrangement may be that by which increased intracranial pressure is relieved by periodic phases of cerebro-spinal rhinorrhoea, as described by Meyer (1905). This form of communication entails however a decided risk of meningeal infection and the modern neurosurgeon would certainly view its existence with disfavour.

Chapter VIII
CONCLUSION

"It is not necessary to study the different works on hydrocephalus very exhaustively to find that actually observed lesions are much rarer than theories explanatory of the causes of hydrocephalus" (Spiller, 1902). The foregoing pages represent an attempt to meet Spiller's reproach. As far as possible the facts have been allowed to speak for themselves and the theories have been allowed to drop into the background. In retrospect it does not appear that much theorizing is demanded, for in practice the common background of hydrocephalus is formed by the single factor of obstruction*, and the immense variety of pathological lesions productive of hydrocephalus have this single feature in common: all create an obstruction at some point in the pathway of the cerebro-spinal fluid.

The mechanism of internal hydrocephalus in the large and varied group of developmental abnormalities is usually obvious. Many of these affect the aqueduct and cause an appreciable reduction of its lumen. Attention has been drawn to the condition often, but erroneously, called "atresia" but preferably, on histological grounds, termed "forking". This is a common cause of congenital hydrocephalus, often associated with spina bifida, but compatible with long survival and minimal hydrocephalus should one of the channels be sufficiently well developed. It has been clearly distinguished from so-called "gliosis" of the aqueduct, the essential pathology of which is a proliferation of the subependymal glia and disruption of the ependyma. Although the ætiology of this is unknown, there are grounds for separating it from the developmental abnormalities and for regarding it as a low-grade inflammatory process. It has been suggested, on the evidence of two cases in which other parts of the ventricular system were examined, that there is a widespread disturbance of the ependyma in this condition, but obstructive effects are limited to the aqueduct on account of its narrowness.

The morphological variations to be found in the Arnold-Chiari malformation have been described: decreasing grades of the deformity accompanied the less severe manifestations of spina bifida. No case has yet been observed in which an Arnold-Chiari malformation has complicated spina bifida occulta. Evidence has been advanced in refutation of the theory that the malformation results from traction from the direction of the spinal cord. While its ætiology remains obscure, it is probable, as Schwalbe and Gredig (1907) originally suggested, that the deformity arises at an early stage of embryogenesis.

No need has been felt for the retention of the term "idiopathic" in connection with hydrocephalus, since no cases have been encountered which could not be explained in terms of one of the categories described in the preceding chapters. To be sure, occasions have arisen, though rarely, in which the intracranial pathology has been so complex as to cloud the sequence of events; such cases have been those in which repeated surgical manœuvres have, as it were, created a smoke-screen through which the nature of the primary disturbance could not clearly be discerned. Haemorrhage, low-grade inflammation and thrombosis have all played a part in such complications. As already indicated the term "idiopathic" has in the past been applied to examples which would now be regarded as post-meningitic. Without question this group, to which the reader's attention has been somewhat lengthily directed, is the most difficult to

* See appendix.

elucidate both clinically and pathologically. But when it is recalled that proved meningococcal meningitis, such as that described in an infant on p. 72, can be followed by gross internal hydrocephalus and yet leave no macroscopic evidence of the attack in the leptomeninges, it is easy to understand how the term "idiopathic" came to be applied to those examples in which the history of an antecedent attack could not be elicited.

The modern chemotherapeutic treatment of infective meningitis saves many lives that would have been lost in former days. But unless treatment is optimal residual lesions must be anticipated; hence it may reasonably be expected to yield a substantial increase in this form of hydrocephalus. Future years will no doubt show whether it does so. Up to date, however, the results of follow-up studies have been gratifying. Thus Maddock (1943) found one case only of hydrocephalus in a series of 1,075 patients who had recovered from cerebro-spinal fever after treatment with sulphonamides. The time, however, between discharge from hospital and the subsequent examination varied from one month to two years: an interval too short for the correct evaluation of hydrocephalus as a sequel. Bailey (1945) quoted four examples of meningitis in infants and young subjects in whom sulphonamides and penicillin seemed to restrain the infection (cultures of the cerebro-spinal fluid being negative), but did not prevent fibroblastic overgrowth and organization of the meninges within a few months of the onset. Obviously, therefore, success in treatment depends upon the institution of vigorous measures at the earliest possible moment. It is possible also that the relatively common gross hydrocephalus of early childhood may come to be substantially reduced in frequency through the recognition and treatment of infantile meningitis. It is now known that this is due to a variety of infective organisms including Gram-negative forms, such as the coliform bacilli, that are exceedingly rare in adult meningitis.

Amongst these various infections syphilis finds little place, if the evidence provided by the present series of cases is accepted as representative of general modern experience. Syphilis indeed has been shown to be a rare cause of severe hydrocephalus; the subjects affected are more likely to be adults.

A controversial form of intracranial hypertension is that which goes by the name of "otitic hydrocephalus". It is to be regretted that, despite experimental and other investigations, this problem still goes unsolved. Two suggestions have been advanced towards a settlement of the controversy. First that it may be essential that the sinus thrombosis should be propagated into the tributary veins in order to produce the clinical syndrome; secondly, that, within limits, expansion of the ventricular system is a reversible change. Observations in support of the latter have been quoted but further investigation is desirable.

ACKNOWLEDGMENTS

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Almost all the photomicrographs were made by Mr. A. J. King, and I should

like to express my appreciation of the skill and care shown both by him and also by my technician, Mr. H. J. Oliver, who was responsible for most of the microscopic preparations. The photographs of gross specimens were made in the photographic departments of the London Hospital and Radcliffe Infirmary respectively, and here too I received welcome co-operation.

TABLE

Normal Circumference of Head from Birth to 14 Years

(From B. Myers: Statistics concerning the height, weight and other measurements of fourteen hundred London children. *Brit. J. Child. Dis.*, 1926, 23, 87)

Age	*Male*		*Female*	
	cm.	*inches*	*cm.*	*Inches*
0 — 1 month	36·0	14·4	35·0	14·0
1 — 2 months	37·9	15·2	37·6	15·0
2 — 3 "	39·0	15·6	38·4	15·4
3 — 4 "	40·0	16·0	39·2	15·7
4 — 5 "	41·7	16·7	40·8	16·3
5 — 6 "	41·9	16·8	41·1	16·4
6 — 9 "	43·5	17·4	44·0	17·6
9 —12 "	45·5	18·2	44·7	17·9
12 —15 "	46·5	18·6	44·9	18·0
15 —18 "	48·1	19·2	46·2	18·5
18 —21 "	47·7	19·1	46·3	18·5
21 —24 "	47·2	18·9	48·3	19·3
2 — 2½ years	49·1	19·6	47·5	19·0
2½— 3 "	48·6	19·4	47·7	19·1
3 — 4 "	49·8	19·9	48·7	19·5
4 — 5 "	49·5	19·8	49·3	19·7
5 — 6 "	50·6	20·2	49·5	19·8
6 — 7 "	50·6	20·2	50·2	20·1
7 — 8 "	51·9	20·8	50·5	20·2
8 — 9 "	51·9	20·8	50·6	20·2
9 —10 "	51·4	20·6	51·2	20·5
10 —11 "	52·3	20·9	51·6	20·6
11 —12 "	52·9	21·2	51·6	20·6
12 —13 "	52·9	21·2	51·9	20·8
13 —14 "	53·6	21·4	52·0	20·8

APPENDIX

HYDROCEPHALUS

This appendix is a reprint of Chapter IX of Volume XXXIV of the Research Publications of the Association for Research in Nervous and Mental Diseases (1954) and is reproduced here by kind permission of the Association. This paper was given by Dorothy S. Russell at the Association's Thirty Fourth Annual Meeting. In the numbering of the figures and table "A.I" corresponds to "IX.I" etc. in the original paper.

ACCEPTING the limitations of our knowledge concerning the precise sites of formation and absorption of cerebro-spinal fluid (C S F.), we are nevertheless faced with the necessity of attempting to explain how internal hydrocephalus may arise. If this condition is defined as one in which the ventricular system of the brain is expanded by C.S.F. under increased pressure, such an expansion could theoretically occur in three possible ways: 1) excessive formation of C.S.F, 2) impairment of its absorption and 3) by an obstruction set up at some point in the pathway of C.S.F. circulation. Table A.1 summarizes the variety of lesions to be included, both observed and hypothetical.

It has already been stated (21) that demonstrable obstruction accounts for an overwhelming majority of observed cases of internal hydrocephalus. The operation of the other two factors is more problematical and hence, at the present time, controversial.

Excessive Formation of C.S.F.

For many years it has been thought likely that the hydrocephalus sometimes associated with choroid-plexus papillomas of the lateral ventricle may be attributable to this factor of over-secretion. The cases recorded have been in infants and young subjects. In the well-known report by Loyal Davis (9) each lateral ventricle contained a tumour-like mass of choroid plexus, the lesion being interpreted as a hypertrophy. In my earlier report I hesitated to accept this mechanism of over-production of C.S.F. as a cause of the hydrocephalus because other possible factors of an obstructive character, in particular post-meningitic adhesions in the basal leptomeninges, had not been specifically excluded in the published reports.

The following case report shows that scepticism in this matter is not devoid of some justification.

Case 1:* A male infant, aged 10 months, developed projectile vomiting and drowsiness 6 days before death, having been previously healthy. There had been a minor injury from a blow in the left parieto-occipital region a few hours before the onset. Four days before death attacks of rigidity affected all limbs and the trunk. On examination the anterior

* Since published by J. F. Smith (23).

TABLE A.1
Causes of Hydrocephalus

A. Obstructive
  I. Maldevelopments
    1. Neural:
      (1) Aqueduct
        (a) Stenosis
        (b) Forking
        (c) Septum
      (2) Foramen of Magendie: septum
      (3) A-C malformation+spina bifida
    2. Meninges: lissencephaly
    3. Skull:
      (1) Platybasia
      (2) Achondroplasia
  II. Gliogenous stenosis of aqueduct (? inflammatory)
  III. Inflammations from exogenous and endogenous particulate matter; from non-bacterial and bacterial organisms.
    1. Obstruction of aqueduct.
    2. Progressive stages of meningitis, and post-meningitic fibrosis.
  IV. Neoplasms in various situations, both intra- and extra-cerebral.
B. Non-obstructive (hypothetical)
  I. Excessive formation of C.S.F.
    1. Papilloma of choroid plexus (lateral ventricle)
    2. Vitamin deficiency (?) } in embryo
    3. Toxins (?) } in embryo
    4. Genetic (?) } in embryo
  II. Defective absorption of C.S.F.: dural sinus thrombosis

fontanelle was tense and pulsating; papilloedema was more marked on the right than the left; the pupils reacted sluggishly to light, and there was nystagmus and deviation of the right eye downwards and medially. The right leg showed slight hypotonia. Tapping of the right lateral ventricle released C.S.F. at a pressure of 500 mm., containing 230 mg. per cent of protein and 2 cells. Ventriculography revealed enlargement of both lateral ventricles and a mass in the left. *Operation*: removal of papilloma of left choroid plexus. The infant died on the following day in hyperpyrexia. *At necropsy*, the lateral and third ventricles were moderately dilated, this being greatest about the site of the tumour. The foramina of Monro were widened (0·5 cm. diam.). The whole ventricular system contained recent blood, and this had escaped into the cisterns of the posterior fossa. Granular ependymitis was conspicuous, especially in the left lateral ventricle (Fig. A.1).

Microscopically this ependymitis is remarkable for its frankly inflammatory appearance, in distinction to the purely glial character of most forms of granular ependymitis. The projecting nodules are of loose spongy tissue, in the meshes of which are a good many mononuclear cells of macrophage type with occasional lymphocytes and polymorph leucocytes and young capillaries (Fig. A.2). The neuroglial stroma is sparse in the majority of these granulations, but in some it is denser and these are less cellular.

Comment. Though we know little of the time required for the evolution of granular ependymitis it is fair to conclude that the process here preceded

FIG. A.1: *Case 1:* Granulations in ependyma of left lateral ventricle. H. and E.×230

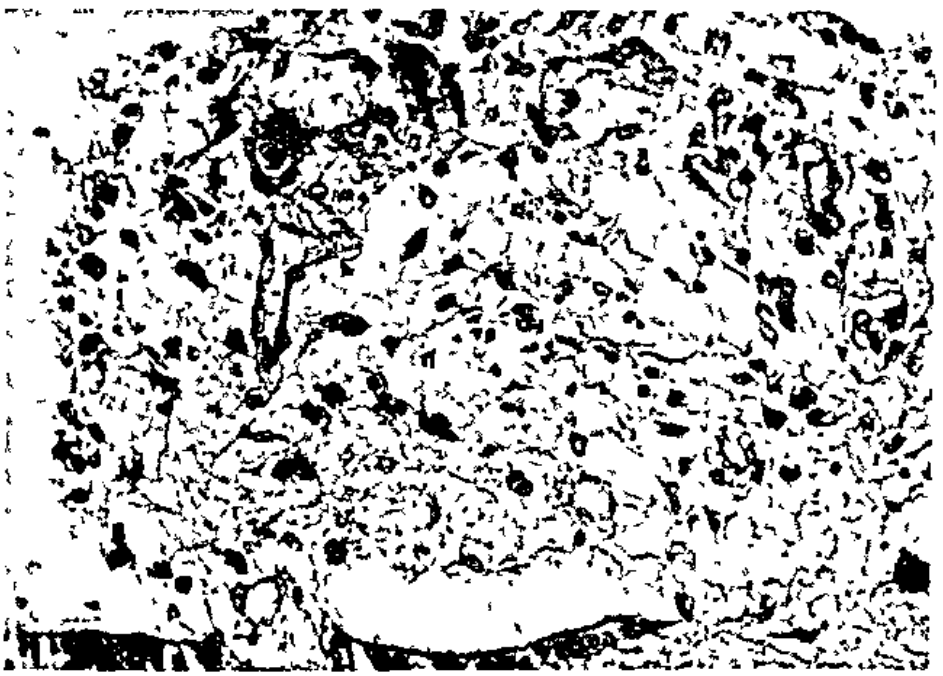

FIG. A.2: *Case 1:* To show vascularisation and inflammatory features of the granulations. H. and E.×330

operation. The low-grade inflammatory character of the reaction strongly suggests the action of an irritant in the CSF, and this is supported by the high protein content of the ventricular fluid That this was elaborated by, or at any rate derived from, the tumour is suggested by the greater development of the ependymitis in the left ventricle than elsewhere. Consequently the attribution of the hydrocephalus to an excessive formation of C.S.F. by the papilloma is vitiated by the demonstration of a low-grade inflammatory process that may well have extended to the basal leptomeninges, promoting there a reaction which could prove obstructive. It is regrettable

that this aspect of the case was not explored. In other examples of a similar kind obstruction of the aqueduct might well occur through granular ependymitis at that level. In parenthisis it should be pointed out that the commoner forms of granular "ependymitis", in which there is no histological evidence of inflammation, can certainly follow internal hydrocephalus, and are best explained in terms of destruction of the ependymal cells from increased pressure and over-reaction of the subjacent neuroglia (21).

On the other hand scepticism concerning the production of hydrocephalus from over-production of C.S.F. is seriously undermined by the two well-documented cases of Kahn and Luros (14), and of Matson (16), in which regression of the hydrocephalus and healthy survival have followed operative removal of the papilloma. As a result there is now wide acceptance of the proposition that over-function of these tumours can promote hydrocephalus. While agreeing that the evidence appears conclusive, it is still difficult to understand the hydrodynamics of such a process. By analogy with other tissues and organs, it might be expected that absorptive apparatus would compensate for any increased demand made upon it. Especially might this be anticipated in view of both the youth of these subjects and the gradual evolution of the syndrome. Again it may be asked why an associated hydrocephalus accompanies only about 50 per cent of papillomas in the lateral ventricle (7). So far no histological criterion is available for the separation of the over-active from the more inert type of papilloma. For the present, therefore, these questions find no answer.

Aside from this postulated over-secretion of C.S.F. by tumours of the choroid plexus, there have been recent suggestions that a mechanism of this kind may be responsible for some forms of congenital hydrocephalus in laboratory animals, when structural anomalies obstructing the flow of C.S.F. have so far not been demonstrated. Such forms of hydrocephalus may be genetic (6), nutritional or toxic. Maternal deprivation of vitamin A has been observed to induce congenital hydrocephalus in the offspring of a strain of rabbits (18). On the other hand, according to a number of short clinical reports (15), hypervitaminosis A is believed to produce a similar, though transitory, effect in human infants. Maternal deficiency of vitamin B_{12}, and possibly also of folic acid, has been held responsible for congenital hydrocephalus in rats (19). Such deficiencies, however, are also known to produce a variety of congenital deformities and, since actual over-secretion by the choroid plexus has not been established in any of these conditions, it is necessary at present to suspend judgment.

Again hydrocephalus has been produced in young rats by serial injections of trypan blue into the mothers before and during pregnancy (10), and this observation is confirmed by Hogan and co-workers (12). It is argued by Gillman that, since the dye is selectively adsorbed by plasma albumin, a metabolic disturbance affects the young and in some way disturbs the relationship between the secretion and absorption of C.S.F. It should be added that, here again, a variety of congenital deformities can be produced by this technique. Thus further work is required in order to eliminate the possibility that structural defects in the brain have been engendered, of such a kind as to obstruct the C.S.F. pathway.

This experimental work, so briefly reviewed, is collectively of interest in suggesting that certain forms of congenital hydrocephalus in human subjects,

now regarded as genetic for lack of a better explanation, may ultimately be attributed to environmental factors affecting maternal metabolism, by analogy with rubella.

Impairment of C.S.F. Absorption

Turning to this even more difficult aspect of C.S.F. hydrodynamics, we face the problem of so-called "otitic hydrocephalus". While there is general recognition of the syndrome of increased intracranial pressure in association with dural sinus-thrombosis, otitic or otherwise, there can be no doubt that ventricular dilatation is an inconstant feature. I have already presented certain evidence, both from the literature and from personal observations, that internal hydrocephalus does occur in some instances. In these there seems *no reasonable alternative explanation of the mechanism other than impairment* of C.S.F. absorption. On the other hand, extensive sinus-thrombosis may be unaccompanied by evidence of raised intracranial pressure; the appearances of internal hydrocephalus may subsequently be found on examination of the brain, but they demand a different interpretation as shown by the following case.

Case 2: M. C., aged 1 year, was well until 5 months before death when convulsive attacks, followed by a right-sided flaccid hemiplegia lasting for about one hour, occurred 2 to 3 times daily. Investigations at another hospital revealed pyrexia (103°F.), leucocytosis (22,000), with a normal C.S.F. Following the use of penicillin the fits ceased, but recurred after 10 days. When admitted to the London Hospital (4 months before death) the child was ill and dehydrated, the anterior fontanelle sunken, head circumference 43·2 cm. (normal for age); 101°F.; fundi and pupils normal; intermittent rapid tremor of left upper eyelid; left facial weakness; ears normal; all limbs hypotonic. The chest and abdomen appeared normal.

Laboratory investigations. C.S.F. of normal composition at pressure of 80 mm.; W.R. negative. Urine: a cloud of albumin. Blood: Hb 79 per cent; W.B.C. 23,500 and, later, 32,400. Blood culture: sterile (6 days after admission).

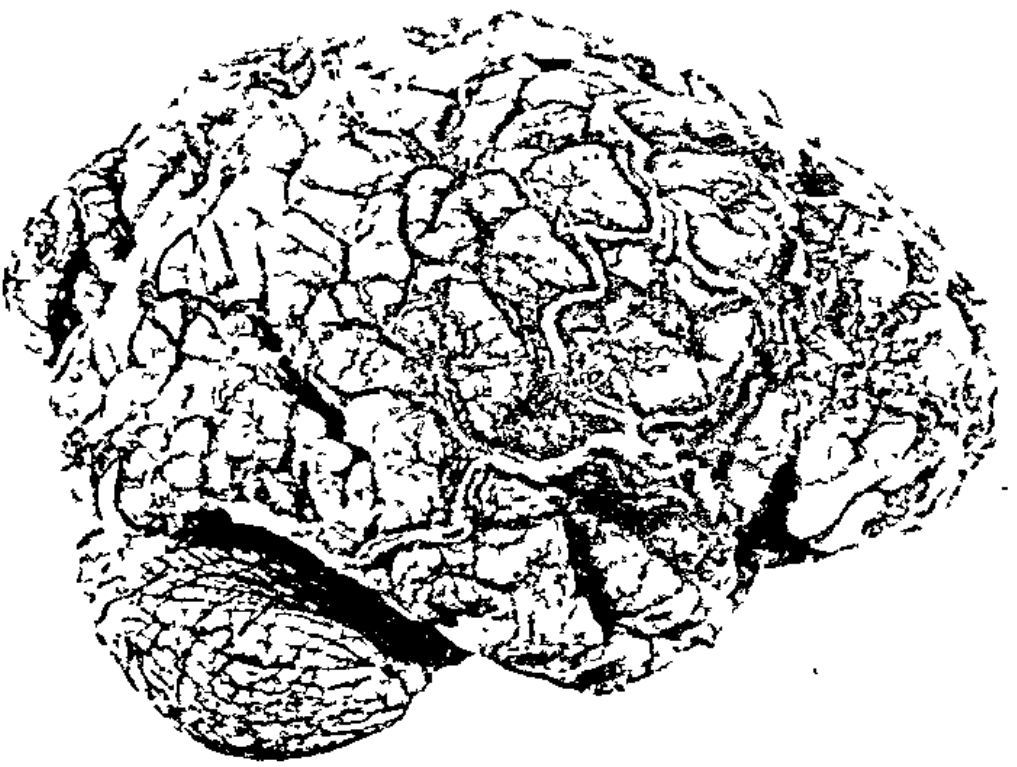

FIG. A.3: *Case 2:* Lateral view of cerebrum showing thrombosis of superior and inferior anastomotic veins

Progress: Mental deterioration and low pyrexia, with occasional unexplained bouts of high fever. Numerous fits, affecting either side of body predominantly at different times. Operative exploration of skull for subdural haematoma was negative. Air encephalograms showed free passage of air over the cerebral hemispheres, but the ventricles were not seen.

Necropsy: Significant findings were limited to the cranium, death being due to broncho pneumonia. Incompletely organized thrombus filled the superior and both lateral sinuses, the remaining sinuses being empty or containing post-mortem clot. Thin patches of partly organized old haemorrhage coated the inner surface of the dura over both cerebral convexities. The superior and inferior anastomotic veins on both sides were

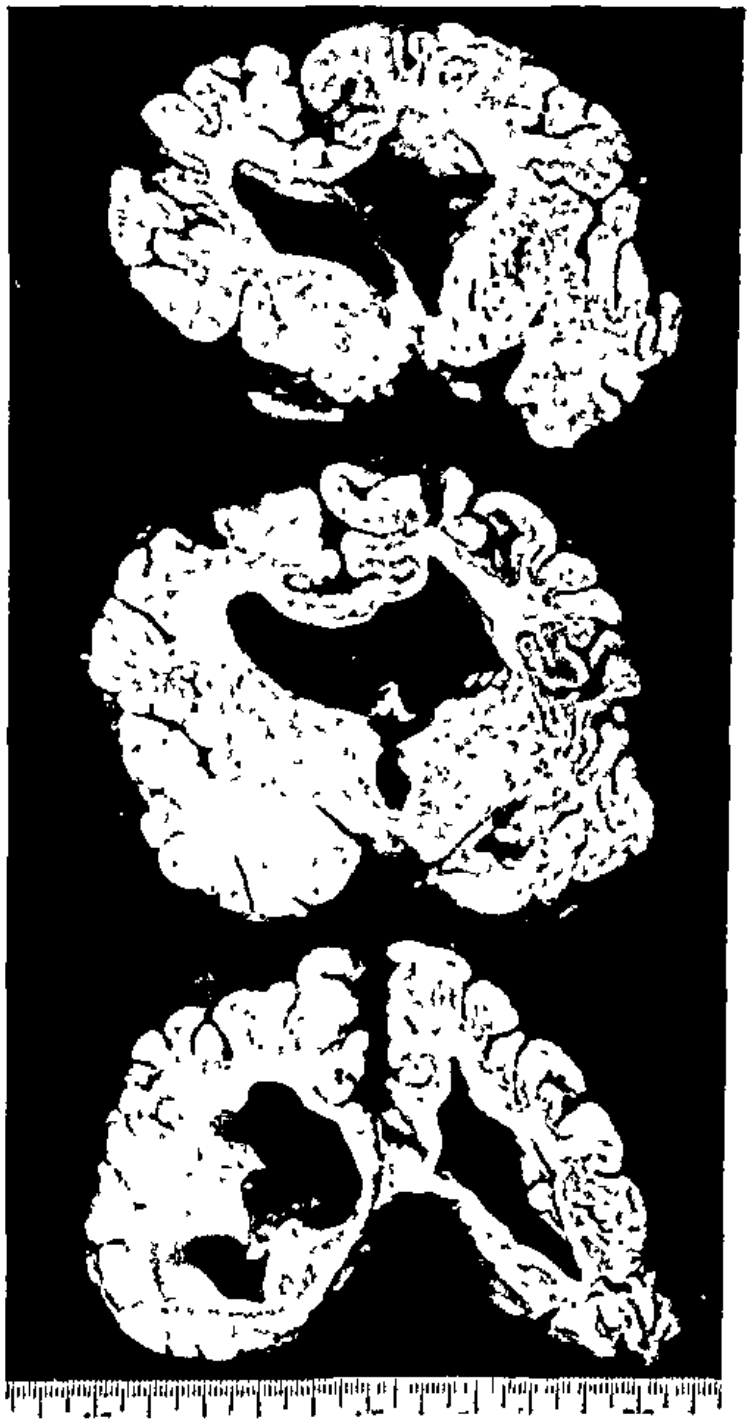

FIG. A.4: *Case 2:* Coronal sections showing ventricular dilatation

distended with ante-mortem thrombus (Fig. A.3). The cerebral vessels and leptomeninges appeared otherwise normal. On coronal section the lateral ventricles were grossly dilated, with fenestration of the septum pellucidum (Fig. A.4) The aqueduct and fourth ventricle were of normal size; the ependyma everywhere was smooth and glistening. The choroid plexuses were small but otherwise not remarkable. There was no visible infarction, or other change in the cerebral substance, though some of the convolutions appeared narrow.

Microscopic examination: Sections from different parts of the superior longitudinal and both lateral sinuses show stages of organization and recanalization of the thrombus at all levels; the process is most advanced, with complete removal of clot, in the central third of the superior longitudinal sinus. By contrast there is little organization in the superior anastomotic veins beyond a few fibroblasts and mononuclear cells in the periphery of the clot. In the inferior anastomotic veins the process is more advanced, though less complete than in the sinuses. The leptomeninges over the brain-stem and cerebral convexities are very sparsely infiltrated with large mononuclear cells and occasional lymphocytes. There are a few patches of extravasated red corpuscles over the cerebrum. Profound anoxic changes of considerable age are irregularly distributed throughout the cerebral cortex and subcortical white matter Apart from inflammation of the pulp of the spleen the examination of other tissues throws no further light on the pathogenesis in this case.

Comment. It may be inferred, from the clinical data, that an initial infection of some kind was responsible for the intracranial sinus-thrombosis The histology suggests that the latter had been of considerable duration and had started in the central third of the superior longitudinal sinus—a segment that is regarded as particularly vulnerable.

In assessing the significance of the ventricular dilatation in this case it must be pointed out that there was no clinical evidence of increased intracranial pressure, and that the weight of the brain was 631 gm (normal for age, 925 gm (8)). Although the appearance of the cerebrum did not suggest any substantial degree of convolutional atrophy there can be little doubt, from the histological evidence of severe focal neuronal degeneration and necrosis, with secondary reactive phenomena, that an anoxic process of wide though uneven distribution was responsible for a diffuse shrinkage of the brain The ventricular dilatation is therefore to be interpreted as a hydrocephalus *e vacuo*, and not a true manifestation of internal hydrocephalus A considerable resemblance exists between this case and case 3 of the report by Bailey and Hass (2). On the other hand their cases 1 and 2 obviously cannot be so explained, since there was clear evidence of increased intracranial pressure, and the hydrocephalus was associated with a brain weight within normal limits.

Well-documented cases are however on record, where sinus-thrombosis has been accompanied by unequivocal evidence of raised intracranial pressure but without ventricular dilatation. To these a further may be added.

Case 3: B. S., male, aged 14. The long and complicated clinical history in this case must be limited to a few salient features. A mild left otitis media, 3½ years before death, was followed by bilateral papilloedema and, on lumbar puncture, normal C.S.F. at a pressure of over 300 mm. was obtained. Ventriculography, a week later, showed normal ventricles; papilloedema persisted at this time. Two weeks later the lumbar C.S F. was under a pressure of 340 mm. and again normal on analysis.

Operation: On account of the patient's deterioration combined ventriculography, arteriography (results of both of these normal), and a right subtemporal decompression were performed by Mr. D. W. C. Northfield 5 weeks after the onset of illness. According to his operation notes the dura was extremely tense and, on opening this, the arachnoid membrane ruptured to emit a spurt of C S F. at least 15 cm. high. This was sustained for "quite a time" and relieved tension. When the dura was opened further the brain bulged but remained intact.

Progress: He improved and was discharged 4 months later. He was readmitted the following year with multiple peripheral thromboses. Despite numerous investigations (including repeated blood-cultures) the cause was unexplained. His final admission, 14 months after this, was for severe haemoptysis which proved fatal after 5 days.
Necropsy: Rupture of an aneurysm of the left pulmonary artery into a bronchus was the cause of death. Sections of many tissues did not disclose the pathogenesis; although polyarteritis nodosa was suspected this diagnosis was not supported histologically. The dural venous sinuses yielded clear macroscopic and microscopic evidence of antecedent thrombosis, both lateral sinuses and the whole length of the superior longitudinal sinus being involved. The thrombus had undergone complete organization with recanalization, the appearances in transverse sections indicating that the entire lumen had certainly been obliterated in the posterior third of the superior longitudinal sinus, but probably only partly occluded elsewhere. The straight sinus was normal. The ventricles of the brain were not dilated, and there was no evidence of infarction.

Comment. The principal interest of this case lies in the observation, at operation, of greatly increased pressure of the C.S.F. in the leptomeninges over the cerebral convexity in conjunction with ventricles of normal size. This appears logical in the circumstances but does nothing to explain the other two categories already mentioned: (a) extensive sinus-thrombosis with no evidence of increased intracranial pressure (see case 2), and (b) similar thrombosis with associated internal hydrocephalus. At the present time, therefore, the problem can be only stated, and there appears to be no working hypothesis which adequately covers the facts. Experimental attempts to reproduce the syndrome of otitic hydrocephalus in various laboratory animals have failed (3), doubtless because these animals have effective mechanisms for the absorption of C.S.F. by way of the olfactory tracts and orbits.

Obstructive Mechanisms in the Aqueduct of Sylvius

It is now proposed to review briefly a few of the many lesions that may obstruct the aqueduct, the selection resting upon those that are perhaps insufficiently recognized, or controversial. It is in this group that the congenital and neo-natal cases of hydrocephalus mostly occur.

Congenital malformations of the aqueduct may be either of the order of a simple stenosis, or what I have already described as "forking".

STENOSIS

Hereditary forms in certain strains of laboratory animals are genetic (11). But it has been claimed by Millen *et al.* that it can also be produced in young rabbits by depriving the does of vitamin A (17). A more recent report (18) of an extension of their work, whereby prolongation of the period of maternal avitaminosis yielded congenital stages of hydrocephalus in the offspring, has entailed second thoughts concerning the mechanism of the hydrocephalus. Thus they now consider it possible that over-secretion of C.S.F. is responsible for this as already mentioned (p. 136), and that the stenosis previously observed at a later stage of the animals' development is somehow secondary. It must be admitted that such a sequence would be contrary to expectation on general principles, but the future unravelling of this problem may well prove of importance in relation to congenital hydrocephalus in man.

So far we do not know why stenosis of the aqueduct occurs in man but it may, at least in some instances, be genetic. This is supported by the report of Bickers and Adams (5), and it is of interest that these authors find that, of 24 published cases of congenital hydrocephalus attributable to stenosis of the aqueduct, 14 subjects had associated malformations elsewhere, especially spina bifida.

The importance, in spina bifida, of a concomitant Arnold-Chiari malformation, occluding the foramen magnum, has been generally recognized within the last decade. In assessing the mechanism of hydrocephalus in such cases it should be remembered that either stenosis or forking of the aqueduct is by *no means uncommon.*

FORKING

The condition is illustrated in Fig. A.5, taken from a transverse section of the mid-brain of an infant aged one month, in whom a sacral meningocele was associated with gross hydrocephalus, and *absence* of the Arnold-Chiari malformation. The aqueduct here is characteristically divided into dorsal

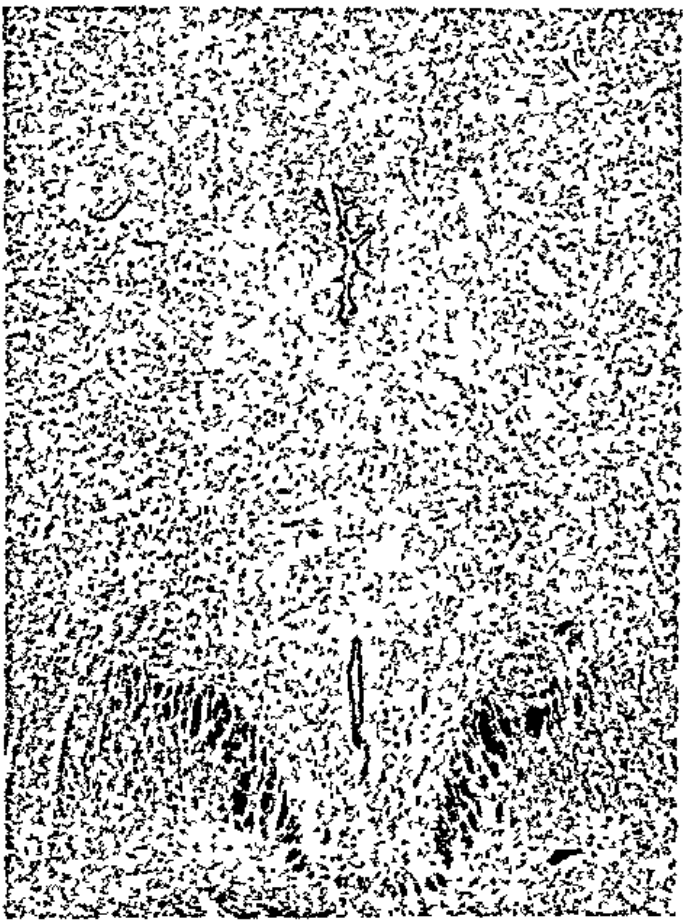

FIG. A.5: Forking of aqueduct associated with sacral meningocele (see text). H. and E. × 16

and ventral components in the mid-line, separated by normal neural tissue, and it may reasonably be inferred that these were functionally inadequate. This case is deliberately selected to reiterate several points germane to the pathogenesis of the Arnold-Chiari malformation: first, that tethering of the cord at the sacral level does not, by traction, cause this malformation. The effect produced by such tethering is in fact a lengthening of the lumbar segments so that the lumbar enlargement is abolished. I have now examined five cases of spina bifida in which the spinal cord was fixed at the sacrum, but in which *no* Arnold-Chiari malformation was found. Secondly that, in hydrocephalus, there is no evidence to prove that pressure upon the neuraxis

from above can produce the Arnold-Chiari malformation by a downward thrust through the foramen magnum. On the contrary the Arnold-Chiari malformation can be demonstrated in the absence of hydrocephalus, where pressure has been relieved by the escape of C.S.F. through a fistula at the site of the spinal defect (22) Tonsillar herniation is the natural outcome of increased pressure from above, and I still question the existence of a genuine Arnold-Chiari malformation in the absence of spina bifida. Furthermore there is evidence that this malformation arises at an early stage of embryogenesis (1) and, if so, it is not necessary to postulate the action of any mechanical force at a later stage

GLIOGENOUS STENOSIS, OR GLIOSIS OF THE AQUEDUCT

The former term, used by Beckett, Netsky and Zimmerman (4), is descriptive of that progressive encroachment upon the lumen by fibrillary neuroglia with, frequently, the subdivision of the aqueduct into many ependymal channels of unequal size which is characteristic of this condition It is essentially different from "forking" of the aqueduct since, in the latter, there is no overgrowth of glia and the tissue separating the two channels is of normal composition If it is agreed that "forking" is a developmental abnormality, there is no such consensus about gliogenous stenosis. Aetiologically the balance is currently suspended between the theories of maldevelopment and inflammation None of the arguments put forward in support of the former stands the weight of criticism On the other hand the inflammatory theory has a good deal in its favour

FIG. A 6: Inflammatory stenosis in association with meningococcal meningitis (see text) H. and E. × 22 approx.

In the first place stenosis of the lumen as a sequel to bacterial infection of the C.S.F. pathway is a recognized cause of hydrocephalus (13, 20). In the case illustrated by Fig. A 6, hydrocephalus followed a meningococcal meningitis in an infant aged 18 weeks. Stenosis is here produced by a young vascularized granulation-tissue rich in mononuclear macrophages, while the ependymal lining has become rolled up into an interrupted circle of small tubules. This circle indicates the original outline of the aqueduct. In this zone, and just internal to it, there is active neuroglial proliferation In conformity with the behaviour of the ependyma in this particular instance it must be conceded that, in all forms of progressive damage to the ventricular lining, these cells *appear inert and incapable of regenerative activity. Thus extensive areas* may become denuded with exposure of the subependymal neuroglia. The latter, however, is certainly capable of active proliferation. As a result the well-known ependymal granulations are formed Adjacent granulations may later fuse, with the production of a continuous sheet of fibrillary neuroglia, deep to which scattered nests of residual ependymal cells provide evidence of the march of events, like fossils in a rock

Such then is the apparent sequence in gliogenous stenosis of the aqueduct But, while this may not be disputed, it may be reasonably argued that no *damaging agent of aetiological significance has been demonstrated in these* cases. The absence of inflammatory cellular infiltration, as well as the negative clinical history, suggests that pathogenic organisms can be ruled out; the

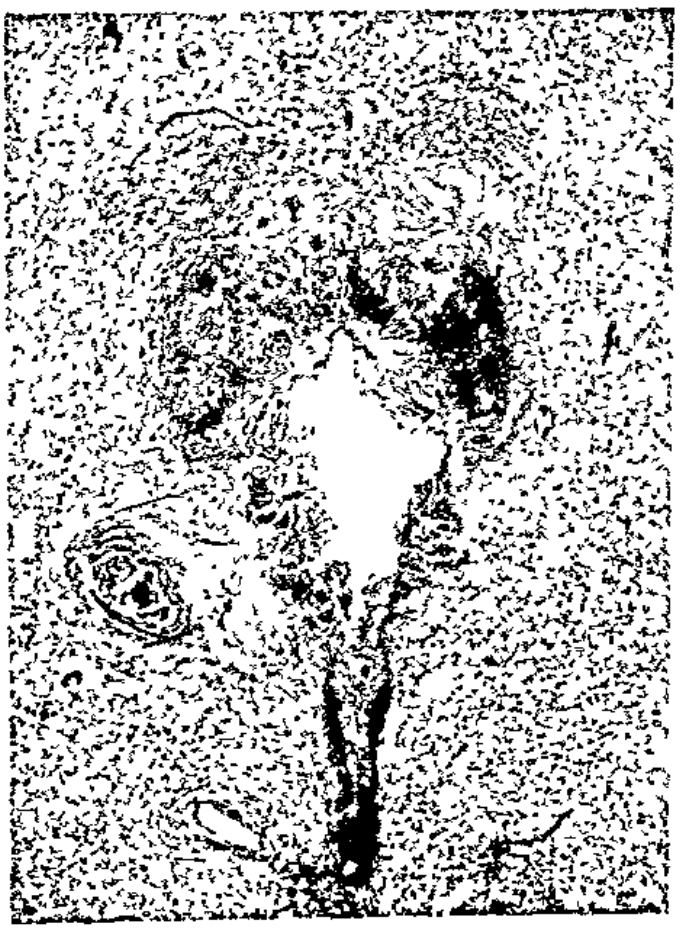

FIG. A.7: *Inflammatory stenosis in association with Boeck's sarcoidosis (see text).* Phosphotungstic-acid haematoxylin × 17

search must be directed elsewhere. As I pointed out in 1949 (21) the involvement of the ependyma in these cases is not restricted to the aqueduct. These observations were however confined at that time to two cases, and the importance of further investigations was emphasized. Recent years have provided no further material of idiopathic gliogenous stenosis for personal investigation. I have, however, two observations upon cases in which a generalized distribution of granular ependymitis was associated with gliogenous changes in the aqueduct which were insufficient to cause internal hydrocephalus. The first (Fig. A.7) is from a man aged 41 who had extensive disseminated sarcoidosis (Boeck) of the brain and meninges. The outline of the lumen of the aqueduct is crenated through the inward bulging of glial cushions, while the ependymal epithelium is restricted to the clefts between them and to some tubules in the left upper quadrant of the field. Foci of Boeck's sarcoid lie near the dorsal wall of the aqueduct, and one is situated at its ventral limit. Cellular infiltration is limited to these foci.

The second case, in a man of 61, is an example of tertiary syphilis. Death was due to an aortic aneurysm. The C.S.F. contained 40 mg. protein and *15 lymphocytes per c.mm.; W.R. positive; Lange 454332. Though there* were no definite clinical features of neurosyphilis the leptomeninges were

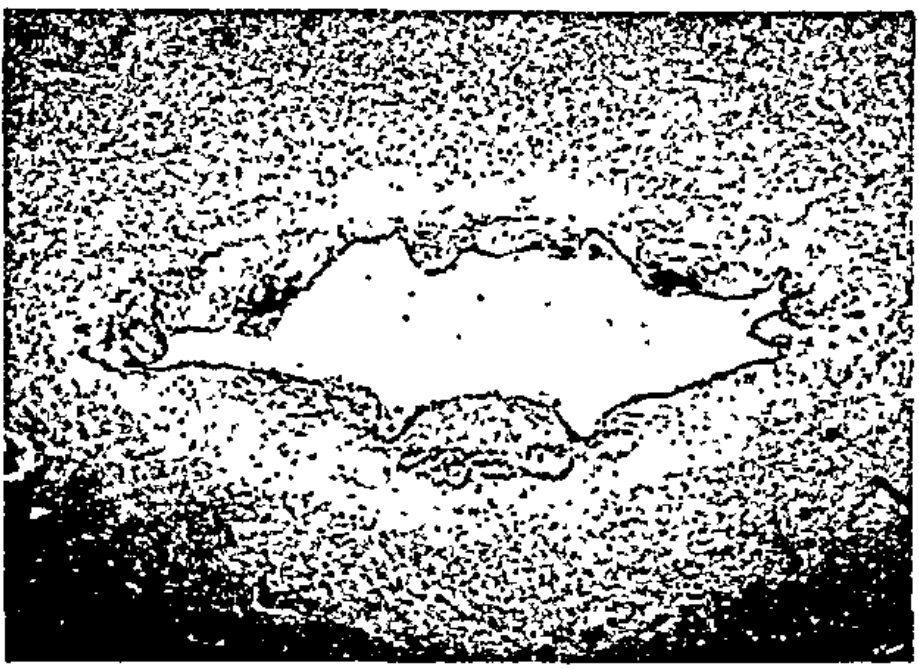

FIG. A.8: Presumed inflammatory stenosis in association with tertiary syphilis (see text). H. and van Gieson. ×22 approx.

slightly opaque and, microscopically, infiltrated rather sparsely with small lymphocytes The aqueduct, sectioned coronally through the superior colliculi, shows a similar though less marked crenation with recession of the ependymal cells (Fig. A.8). There is no inflammatory cellular infiltration.

These two examples have been quoted in conjunction with that of meningococcal infection to illustrate the gradations of inflammatory reaction where

the aetiology can be defined. That they have points in common with gliogenous stenosis (Fig. A.9) cannot be denied, and it may reasonably be argued that the inflammatory hypothesis has, at the present time, the better claim for support.

FIG. A.9: Idiopathic gliogenous stenosis of aqueduct. Phosphotungstic-acid haematoxylin. × 30
(*This figure is the same as Fig.* 26 *on p.* 45)

DISCUSSION

PRESIDENT MCINTOSH: Dr. Donald D. Matson of Boston has raised this question: "Has Dr. Russell seen more than the one case she illustrated of hydrocephalus associated with spina bifida in which aqueduct stenosis without the Arnold-Chiari malformation was the cause of the internal hydrocephalus?"

DR. DOROTHY S. RUSSELL: I have seen stenosis of the aqueduct in several cases of sacral meningocele or spina bifida occulta, in which there was no Arnold-Chiari malformation; also, one has seen it frequently with the much more common myelomeningoceles, in which, of course, there is a wide distribution of various developmental defects.

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